

concentrations of the fusion protein to be tested. Cells are suspended at a concentration of 2×10^6 /ml in PBS containing PI at a final concentration of 5 μ g/ml, and then incubated at room temperature for 5 minutes before FACScan analysis. PI uptake has been demonstrated to correlate with DNA fragmentation in this experimental paradigm.

[0971] Effect on cytokine release. An important function of monocytes/macrophages is their regulatory activity on other cellular populations of the immune system through the release of cytokines after stimulation. An ELISA to measure cytokine release is performed as follows. Human monocytes are incubated at a density of 5×10^5 cells/ml with increasing concentrations of an albumin fusion protein of the invention and under the same conditions, but in the absence of the fusion protein. For IL-12 production, the cells are primed overnight with IFN (100 U/ml) in the presence of the fusion protein. LPS (10 ng/ml) is then added. Conditioned media are collected after 24h and kept frozen until use. Measurement of TNF-alpha, IL-10, MCP-1 and IL-8 is then performed using a commercially available ELISA kit (e.g., R & D Systems (Minneapolis, MN)) and applying the standard protocols provided with the kit.

[0972] Oxidative burst. Purified monocytes are plated in 96-w plate at 2×10^5 cell/well. Increasing concentrations of an albumin fusion protein of the invention are added to the wells in a total volume of 0.2 ml culture medium (RPMI 1640 + 10% FCS, glutamine and antibiotics). After 3 days incubation, the plates are centrifuged and the medium is removed from the wells. To the macrophage monolayers, 0.2 ml per well of phenol red solution (140 mM NaCl, 10 mM potassium phosphate buffer pH 7.0, 5.5 mM dextrose, 0.56 mM phenol red and 19 U/ml of HRPO) is added, together with the stimulant (200 nM PMA). The plates are incubated at 37°C for 2 hours and the reaction is stopped by adding 20 μ l 1N NaOH per well. The absorbance is read at 610 nm. To calculate the amount of H_2O_2 produced by the macrophages, a standard curve of a H_2O_2 solution of known molarity is performed for each experiment.

EXAMPLE 19: The Effect of Albumin Fusion Proteins of the Invention on the Growth of Vascular Endothelial Cells.

[0973] On day 1, human umbilical vein endothelial cells (HUVEC) are seeded at 2×10^4 cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin, and 50 units/ml endothelial cell growth supplements (ECGS, Biotechnology, Inc.). On day 2, the medium is replaced with M199 containing 10% FBS, 8

units/ml heparin. An albumin fusion protein of the invention, and positive controls, such as VEGF and basic FGF (bFGF) are added, at varying concentrations. On days 4 and 6, the medium is replaced. On day 8, cell number is determined with a Coulter Counter.

[0974] An increase in the number of HUVEC cells indicates that the fusion protein may proliferate vascular endothelial cells, while a decrease in the number of HUVEC cells indicates that the fusion protein inhibits vascular endothelial cells.

EXAMPLE 20: Rat Corneal Wound Healing Model.

[0975] This animal model shows the effect of an albumin fusion protein of the invention on neovascularization. The experimental protocol includes:

Making a 1-1.5 mm long incision from the center of cornea into the stromal layer.

Inserting a spatula below the lip of the incision facing the outer corner of the eye.

Making a pocket (its base is 1-1.5 mm from the edge of the eye).

Positioning a pellet, containing 50ng- 5ug of an albumin fusion protein of the invention, within the pocket.

[0976] Treatment with an an albumin fusion protein of the invention can also be applied topically to the corneal wounds in a dosage range of 20mg - 500mg (daily treatment for five days).

EXAMPLE 21: Diabetic Mouse and Glucocorticoid-Impaired Wound Healing Models.

Diabetic db+/db+ Mouse Model.

[0977] To demonstrate that an albumin fusion protein of the invention accelerates the healing process, the genetically diabetic mouse model of wound healing is used. The full thickness wound healing model in the db+/db+ mouse is a well characterized, clinically relevant and reproducible model of impaired wound healing. Healing of the diabetic wound is dependent on formation of granulation tissue and re-epithelialization rather than contraction (Gartner, M.H. *et al.*, *J. Surg. Res.* 52:389 (1992); Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)).

[0978] The diabetic animals have many of the characteristic features observed in Type II diabetes mellitus. Homozygous (db+/db+) mice are obese in comparison to their normal heterozygous (db+/+m) littermates. Mutant diabetic (db+/db+) mice have a single autosomal recessive mutation on chromosome 4 (db+) (Coleman *et al.* *Proc. Natl. Acad. Sci. USA* 77:283-293 (1982)). Animals show polyphagia, polydipsia and polyuria. Mutant diabetic

mice (db+/db+) have elevated blood glucose, increased or normal insulin levels, and suppressed cell-mediated immunity (Mandel *et al.*, *J. Immunol.* 120:1375 (1978); Debray-Sachs, M. *et al.*, *Clin. Exp. Immunol.* 51(1):1-7 (1983); Leiter *et al.*, *Am. J. of Pathol.* 114:46-55 (1985)). Peripheral neuropathy, myocardial complications, and microvascular lesions, basement membrane thickening and glomerular filtration abnormalities have been described in these animals (Norido, F. *et al.*, *Exp. Neurol.* 83(2):221-232 (1984); Robertson *et al.*, *Diabetes* 29(1):60-67 (1980); Giacomelli *et al.*, *Lab Invest.* 40(4):460-473 (1979); Coleman, D.L., *Diabetes* 31 (Suppl):1-6 (1982)). These homozygous diabetic mice develop hyperglycemia that is resistant to insulin analogous to human type II diabetes (Mandel *et al.*, *J. Immunol.* 120:1375-1377 (1978)).

[0979] The characteristics observed in these animals suggests that healing in this model may be similar to the healing observed in human diabetes (Greenhalgh, *et al.*, *Am. J. of Pathol.* 136:1235-1246 (1990)).

[0980] Genetically diabetic female C57BL/KsJ (db+/db+) mice and their non-diabetic (db+/+m) heterozygous littermates are used in this study (Jackson Laboratories). The animals are purchased at 6 weeks of age and are 8 weeks old at the beginning of the study. Animals are individually housed and received food and water ad libitum. All manipulations are performed using aseptic techniques. The experiments are conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

[0981] Wounding protocol is performed according to previously reported methods (Tsuboi, R. and Rifkin, D.B., *J. Exp. Med.* 172:245-251 (1990)). Briefly, on the day of wounding, animals are anesthetized with an intraperitoneal injection of Avertin (0.01 mg/mL), 2,2,2-tribromoethanol and 2-methyl-2-butanol dissolved in deionized water. The dorsal region of the animal is shaved and the skin washed with 70% ethanol solution and iodine. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is then created using a Keyes tissue punch. Immediately following wounding, the surrounding skin is gently stretched to eliminate wound expansion. The wounds are left open for the duration of the experiment. Application of the treatment is given topically for 5 consecutive days commencing on the day of wounding. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

[0982] Wounds are visually examined and photographed at a fixed distance at the day of surgery and at two day intervals thereafter. Wound closure is determined by daily

measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

[0983] An albumin fusion protein of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

[0984] Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology and immunohistochemistry. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

[0985] Three groups of 10 animals each (5 diabetic and 5 non-diabetic controls) are evaluated: 1) Vehicle placebo control, 2) untreated group, and 3) treated group.

[0986] Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total square area of the wound. Contraction is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

$$a. \text{ [Open area on day 8] - [Open area on day 1] / [Open area on day 1]}$$

[0987] Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using a Reichert-Jung microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds are used to assess whether the healing process and the morphologic appearance of the repaired skin is altered by treatment with an albumin fusion protein of the invention. This assessment included verification of the presence of cell accumulation, inflammatory cells, capillaries, fibroblasts, re-epithelialization and epidermal maturity (Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)). A calibrated lens micrometer is used by a blinded observer.

[0988] Tissue sections are also stained immunohistochemically with a polyclonal rabbit anti-human keratin antibody using ABC Elite detection system. Human skin is used as a positive tissue control while non-immune IgG is used as a negative control. Keratinocyte growth is determined by evaluating the extent of reepithelialization of the wound using a

calibrated lens micrometer.

[0989] Proliferating cell nuclear antigen/cyclin (PCNA) in skin specimens is demonstrated by using anti-PCNA antibody (1:50) with an ABC Elite detection system. Human colon cancer served as a positive tissue control and human brain tissue is used as a negative tissue control. Each specimen included a section with omission of the primary antibody and substitution with non-immune mouse IgG. Ranking of these sections is based on the extent of proliferation on a scale of 0-8, the lower side of the scale reflecting slight proliferation to the higher side reflecting intense proliferation.

[0990] Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

Steroid Impaired Rat Model

[0991] The inhibition of wound healing by steroids has been well documented in various *in vitro* and *in vivo* systems (Wahl, Glucocorticoids and Wound healing. In: Anti-Inflammatory Steroid Action: Basic and Clinical Aspects. 280-302 (1989); Wahl *et al.*, *J. Immunol.* 115: 476-481 (1975); Werb *et al.*, *J. Exp. Med.* 147:1684-1694 (1978)). Glucocorticoids retard wound healing by inhibiting angiogenesis, decreasing vascular permeability (Ebert *et al.*, *Am. Intern. Med.* 37:701-705 (1952)), fibroblast proliferation, and collagen synthesis (Beck *et al.*, *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978)) and producing a transient reduction of circulating monocytes (Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989)). The systemic administration of steroids to impaired wound healing is a well establish phenomenon in rats (Beck *et al.*, *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989); Pierce *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 2229-2233 (1989)).

[0992] To demonstrate that an albumin fusion protein of the invention can accelerate the healing process, the effects of multiple topical applications of the fusion protein on full thickness excisional skin wounds in rats in which healing has been impaired by the systemic administration of methylprednisolone is assessed.

[0993] Young adult male Sprague Dawley rats weighing 250-300 g (Charles River

Laboratories) are used in this example. The animals are purchased at 8 weeks of age and are 9 weeks old at the beginning of the study. The healing response of rats is impaired by the systemic administration of methylprednisolone (17mg/kg/rat intramuscularly) at the time of wounding. Animals are individually housed and received food and water *ad libitum*. All manipulations are performed using aseptic techniques. This study is conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

[0994] The wounding protocol is followed according to that described above. On the day of wounding, animals are anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (5 mg/kg). The dorsal region of the animal is shaved and the skin washed with 70% ethanol and iodine solutions. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is created using a Keyes tissue punch. The wounds are left open for the duration of the experiment. Applications of the testing materials are given topically once a day for 7 consecutive days commencing on the day of wounding and subsequent to methylprednisolone administration. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

[0995] Wounds are visually examined and photographed at a fixed distance at the day of wounding and at the end of treatment. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

[0996] The fusion protein of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

[0997] Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

[0998] Three groups of 10 animals each (5 with methylprednisolone and 5 without glucocorticoid) are evaluated: 1) Untreated group 2) Vehicle placebo control 3) treated groups.

[0999] Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total area of the wound. Closure is then estimated by establishing the

differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm^2 , the corresponding size of the dermal punch. Calculations are made using the following formula:

$$\text{b. } [\text{Open area on day 8}] - [\text{Open area on day 1}] / [\text{Open area on day 1}]$$

[1000] Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using an Olympus microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds allows assessment of whether the healing process and the morphologic appearance of the repaired skin is improved by treatment with an albumin fusion protein of the invention. A calibrated lens micrometer is used by a blinded observer to determine the distance of the wound gap.

[1001] Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

EXAMPLE 22: Lymphedema Animal Model.

[1002] The purpose of this experimental approach is to create an appropriate and consistent lymphedema model for testing the therapeutic effects of an albumin fusion protein of the invention in lymphangiogenesis and re-establishment of the lymphatic circulatory system in the rat hind limb. Effectiveness is measured by swelling volume of the affected limb, quantification of the amount of lymphatic vasculature, total blood plasma protein, and histopathology. Acute lymphedema is observed for 7-10 days. Perhaps more importantly, the chronic progress of the edema is followed for up to 3-4 weeks.

[1003] Prior to beginning surgery, blood sample is drawn for protein concentration analysis. Male rats weighing approximately ~350g are dosed with Pentobarbital. Subsequently, the right legs are shaved from knee to hip. The shaved area is swabbed with gauze soaked in 70% EtOH. Blood is drawn for serum total protein testing. Circumference and volumetric measurements are made prior to injecting dye into paws after marking 2 measurement levels (0.5 cm above heel, at mid-pt of dorsal paw). The intradermal dorsum of both right and left paws are injected with 0.05 ml of 1% Evan's Blue. Circumference and volumetric measurements are then made following injection of dye into paws.

[1004] Using the knee joint as a landmark, a mid-leg inguinal incision is made

circumferentially allowing the femoral vessels to be located. Forceps and hemostats are used to dissect and separate the skin flaps. After locating the femoral vessels, the lymphatic vessel that runs along side and underneath the vessel(s) is located. The main lymphatic vessels in this area are then electrically coagulated or suture ligated.

[1005] Using a microscope, muscles in back of the leg (near the semitendinosus and adductors) are bluntly dissected. The popliteal lymph node is then located. The 2 proximal and 2 distal lymphatic vessels and distal blood supply of the popliteal node are then ligated by suturing. The popliteal lymph node, and any accompanying adipose tissue, is then removed by cutting connective tissues.

[1006] Care is taken to control any mild bleeding resulting from this procedure. After lymphatics are occluded, the skin flaps are sealed by using liquid skin (Vetbond) (AJ Buck). The separated skin edges are sealed to the underlying muscle tissue while leaving a gap of ~0.5 cm around the leg. Skin also may be anchored by suturing to underlying muscle when necessary.

[1007] To avoid infection, animals are housed individually with mesh (no bedding). Recovering animals are checked daily through the optimal edematous peak, which typically occurred by day 5-7. The plateau edematous peak are then observed. To evaluate the intensity of the lymphedema, the circumference and volumes of 2 designated places on each paw before operation and daily for 7 days are measured. The effect of plasma proteins on lymphedema is determined and whether protein analysis is a useful testing perimeter is also investigated. The weights of both control and edematous limbs are evaluated at 2 places. Analysis is performed in a blind manner.

[1008] Circumference Measurements: Under brief gas anesthetic to prevent limb movement, a cloth tape is used to measure limb circumference. Measurements are done at the ankle bone and dorsal paw by 2 different people and those 2 readings are averaged. Readings are taken from both control and edematous limbs.

[1009] Volumetric Measurements: On the day of surgery, animals are anesthetized with Pentobarbital and are tested prior to surgery. For daily volumetrics animals are under brief halothane anesthetic (rapid immobilization and quick recovery), and both legs are shaved and equally marked using waterproof marker on legs. Legs are first dipped in water, then dipped into instrument to each marked level then measured by Buxco edema software(Chen/Victor). Data is recorded by one person, while the other is dipping the limb to marked area.

[1010] Blood-plasma protein measurements: Blood is drawn, spun, and serum separated prior to surgery and then at conclusion for total protein and Ca^{2+} comparison.

[1011] Limb Weight Comparison: After drawing blood, the animal is prepared for tissue collection. The limbs are amputated using a quillitine, then both experimental and control legs are cut at the ligature and weighed. A second weighing is done as the tibio-cacaneal joint is disarticulated and the foot is weighed.

[1012] Histological Preparations: The transverse muscle located behind the knee (popliteal) area is dissected and arranged in a metal mold, filled with freezeGel, dipped into cold methylbutane, placed into labeled sample bags at - 80EC until sectioning. Upon sectioning, the muscle is observed under fluorescent microscopy for lymphatics..

EXAMPLE 23: Suppression of TNF alpha-Induced Adhesion Molecule Expression by an Albumin Fusion Protein of the Invention.

[1013] The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

[1014] Tumor necrosis factor alpha (TNF-a), a potent proinflammatory cytokine, is a stimulator of all three CAMs on endothelial cells and may be involved in a wide variety of inflammatory responses, often resulting in a pathological outcome.

[1015] The potential of an albumin fusion protein of the invention to mediate a suppression of TNF-a induced CAM expression can be examined. A modified ELISA assay which uses ECs as a solid phase absorbent is employed to measure the amount of CAM expression on TNF-a treated ECs when co-stimulated with a member of the FGF family of proteins.

[1016] To perform the experiment, human umbilical vein endothelial cell (HUVEC) cultures are obtained from pooled cord harvests and maintained in growth medium (EGM-2;

Clonetics, San Diego, CA) supplemented with 10% FCS and 1% penicillin/streptomycin in a 37 degree C humidified incubator containing 5% CO₂. HUVECs are seeded in 96-well plates at concentrations of 1×10^4 cells/well in EGM medium at 37 degree C for 18-24 hrs or until confluent. The monolayers are subsequently washed 3 times with a serum-free solution of RPMI-1640 supplemented with 100 U/ml penicillin and 100 mg/ml streptomycin, and treated with a given cytokine and/or growth factor(s) for 24 h at 37 degree C. Following incubation, the cells are then evaluated for CAM expression.

[1017] Human Umbilical Vein Endothelial cells (HUVECs) are grown in a standard 96 well plate to confluence. Growth medium is removed from the cells and replaced with 90 μ l of 199 Medium (10% FBS). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 μ l volumes). Plates are incubated at 37 degree C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 μ l of 0.1% paraformaldehyde-PBS(with Ca⁺⁺ and Mg⁺⁺) is added to each well. Plates are held at 4°C for 30 min.

[1018] Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. Add 10 μ l of diluted primary antibody to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 μ g/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA.

[1019] Then add 20 μ l of diluted ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution) to each well and incubated at 37°C for 30 min. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 ml of glycine buffer (pH 10.4). 100 μ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: $1:5,000 (10^0) > 10^{-0.5} > 10^{-1} > 10^{-1.5}$. 5 μ l of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 μ l of pNPP reagent must then be added to each of the standard wells. The plate must be incubated at 37°C for 4h. A volume of 50 μ l of 3M NaOH is added to all wells. The results are quantified on a plate reader at 405 nm. The background subtraction option is used on blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng;

0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

EXAMPLE 24: Construction of GAS Reporter Construct.

[1020] One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

[1021] GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

[1022] The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

[1023] The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995)). A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:53)).

[1024] Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway. Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example,

growth factors and cytokines are known to activate the Jaks-STATs pathway (See Table 5, below). Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

Table 5

<u>JAKs</u>	<u>STATS</u>				<u>GAS(elements) or ISRE</u>	
<u>Ligand</u>	<u>tyk2</u>	<u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>		
<u>IFN family</u>						
IFN-a/B	+	+	-	-	1,2,3	ISRE
IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
Il-10	+	?	?	-	1,3	
<u>gp130 family</u>						
IL-6 (Pleiotropic)	+	+	+	?	1,3	GAS(IRF1>Lys6>IFP)
Il-11(Pleiotropic)	?	+	?	?	1,3	
OnM(Pleiotropic)	?	+	+	?	1,3	
LIF(Pleiotropic)	?	+	+	?	1,3	
CNTF(Pleiotropic)	-/+	+	+	?	1,3	
G-CSF(Pleiotropic)	?	+	?	?	1,3	
IL-12(Pleiotropic)	+	-	+	+	1,3	
<u>g-C family</u>						
IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
IL-4 (lymph/myeloid)	-	+	-	+	6	GAS(IRF1=IFP>>Ly6)(IgH)
IL-7 (lymphocytes)	-	+	-	+	5	GAS
IL-9 (lymphocytes)	-	+	-	+	5	GAS
IL-13 (lymphocyte)	-	+	?	?	6	GAS
IL-15	?	+	?	+	5	GAS
<u>gp140 family</u>						
IL-3 (myeloid)	-	-	+	-	5	GAS(IRF1>IFP>>Ly6)
IL-5 (myeloid)	-	-	+	-	5	GAS
GM-CSF (myeloid)	-	-	+	-	5	GAS
<u>Growth hormone family</u>						
GH	?	-	+	-	5	
PRL	?	+/-	+	-	1,3,5	
EPO	?	-	+	-	5	GAS (B-CAS>IRF1=IFP>>Ly6)
<u>Receptor Tyrosine Kinases</u>						
EGF	?	+	+	-	1,3	GAS (IRF1)
PDGF	?	+	+	-	1,3	
CSF-1	?	+	+	-	1,3	GAS(not IRF1)

[1025] To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 27-29, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

5':GCGCCTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATGATTTCCTCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:54)

[1026] The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO:55)

[1027] PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCATCCCGCCCCTAACTCCGCCAGTTCCGCCATTCTCCGCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCTCGGCCTCTGAGCTATTCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT:3' (SEQ ID NO:56)

[1028] With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

[1029] The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to

create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

[1030] Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using Sall and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 27-29.

[1031] Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing EGR and NF-KB promoter sequences are described in Examples 27-31. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

EXAMPLE 25: Assay for SEAP Activity.

[1032] As a reporter molecule for the assays described in examples disclosed herein, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

[1033] Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 ul of 2.5x dilution buffer into Optiplates containing 35 ul of a solution containing an albumin fusion protein of the invention. Seal the plates with a plastic sealer and incubate at 65 degree C for 30 min. Separate the Optiplates to avoid uneven heating.

[1034] Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 ml Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the Table below). Add 50 ul Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on a luminometer, thus one should treat 5 plates at each time and start the second set 10

minutes later.

[1035] Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Table 6

# of plates	Rxn buffer diluent (ml)	CSPD (ml)	# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3	31	165	8.25
11	65	3.25	32	170	8.5
12	70	3.5	33	175	8.75
13	75	3.75	34	180	9
14	80	4	35	185	9.25
15	85	4.25	36	190	9.5
16	90	4.5	37	195	9.75
17	95	4.75	38	200	10
18	100	5	39	205	10.25
19	105	5.25	40	210	10.5
20	110	5.5	41	215	10.75
21	115	5.75	42	220	11
22	120	6	43	225	11.25
23	125	6.25	44	230	11.5
24	130	6.5	45	235	11.75
25	135	6.75	46	240	12
26	140	7	47	245	12.25
27	145	7.25	48	250	12.5
28	150	7.5	49	255	12.75
29	155	7.75	50	260	13
30	160	8			

EXAMPLE 26: Assay Identifying Neuronal Activity.

[1036] When cells undergo differentiation and proliferation, a group of genes are

activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, the ability of fusion proteins of the invention to activate cells can be assessed.

[1037] Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells by an albumin fusion protein of the present invention can be assessed.

[1038] The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

First primer: 5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG-3' (SEQ ID NO:57)

Second primer: 5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:58)

[1039] Using the GAS:SEAP/Neo vector produced in Example 24, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

[1040] To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

[1041] PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up

and down for more than 15 times.

[1042] Transfect the EGR/SEAP/Neo construct into PC12 using techniques known in the art. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

[1043] To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

[1044] The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as 5×10^5 cells/ml.

[1045] Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1×10^5 cells/well). Add a series of different concentrations of an albumin fusion protein of the invention, 37 degree C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay may be routinely performed using techniques known in the art and/or as described in Example 25.

EXAMPLE 27: Assay for T-cell Activity.

[1046] The following protocol is used to assess T-cell activity by identifying factors, and determining whether an albumin fusion protein of the invention proliferates and/or differentiates T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 75. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

[1047] Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The

transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

[1048] Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 μ l of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies) with 10 μ g of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 μ l of DMRIE-C and incubate at room temperature for 15-45 mins.

[1049] During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final concentration of 10^7 cells/ml. Then add 1ml of 1×10^7 cells in OPTI-MEM to T25 flask and incubate at 37 degree C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

[1050] The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Gentamicin, and 1% Pen-Strep. These cells are treated with varying concentrations of one or more fusion proteins of the present invention.

[1051] On the day of treatment with the fusion protein, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of fusion proteins and the number of different concentrations of fusion proteins being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

[1052] The well dishes containing Jurkat cells treated with the fusion protein are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 μ l samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophane covers) and stored at -20 degree C until SEAP assays are performed according to Example 25. The plates containing the remaining treated cells are placed at 4 degree C and serve as a source of material for repeating the assay on a specific well if desired.

[1053] As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

[1054] The above protocol may be used in the generation of both transient, as well as, stable transfected cells, which would be apparent to those of skill in the art.

EXAMPLE 28: Assay for T-cell Activity.

[1055] NF-KB (Nuclear Factor KB) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-KB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF-KB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

[1056] In non-stimulated conditions, NF-KB is retained in the cytoplasm with I-KB (Inhibitor KB). However, upon stimulation, I-KB is phosphorylated and degraded, causing NF-KB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF-KB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

[1057] Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-KB promoter element are used to screen the fusion protein. Activators or inhibitors of NF-KB would be useful in treating, preventing, and/or diagnosing diseases. For example, inhibitors of NF-KB could be used to treat those diseases related to the acute or chronic activation of NF-KB, such as rheumatoid arthritis.

[1058] To construct a vector containing the NF-KB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-KB binding site (GGGGACTTTCCC) (SEQ ID NO:59), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTC
CATCCTGCCATCTCAATTAG:3' (SEQ ID NO:60)

[1059] The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO:55)

[1060] PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with

the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCCATCTG
CCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCC
CTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTAT
TTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGG
AGGCTTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT:3' (SEQ ID NO:61)

[1061] Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-KB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

[1062] In order to generate stable mammalian cell lines, the NF-KB/SV40/SEAP cassette is removed from the above NF-KB/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF-KB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

[1063] Once NF-KB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 25. Similarly, the method for assaying fusion proteins with these stable Jurkat T-cells is also described in Example 25. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

EXAMPLE 29: Assay Identifying Myeloid Activity.

[1064] The following protocol is used to assess myeloid activity of an albumin fusion protein of the present invention by determining whether the fusion protein proliferates and/or differentiates myeloid cells. Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 24. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

[1065] To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 24, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2×10^7 U937 cells and wash with PBS. The

U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

[1066] Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM Na₂HPO₄·7H₂O, 1 mM MgCl₂, and 675 uM CaCl₂. Incubate at 37 degrees C for 45 min.

[1067] Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37 degree C for 36 hr.

[1068] The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

[1069] These cells are tested by harvesting 1×10^8 cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of 5×10^5 cells/ml. Plate 200 ul cells per well in the 96-well plate (or 1×10^5 cells/well).

[1070] Add different concentrations of the fusion protein. Incubate at 37 degree C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to methods known in the art and/or the protocol described in Example 25.

EXAMPLE 30: Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability.

[1071] Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify fusion proteins which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

[1072] The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules.

Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

[1073] For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

[1074] A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4, 50 ul of 12 ug/ml fluo-4 is added to each well. The plate is incubated at 37 degrees C in a CO₂ incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

[1075] For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10⁶ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37 degrees C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10⁶ cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley Cell Wash with 200 ul, followed by an aspiration step to 100 ul final volume.

[1076] For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-4. The fusion protein of the invention is added to the well, and a change in fluorescence is detected.

[1077] To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event caused by an albumin fusion protein of the present invention or a molecule induced by an albumin fusion protein of the present invention, which has resulted in an increase in the intracellular Ca⁺⁺ concentration.

EXAMPLE 31: Assay Identifying Tyrosine Kinase Activity.

[1078] The Protein Tyrosine Kinases (PTK) represent a diverse group of

transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase (RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

[1079] Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

[1080] Because of the wide range of known factors capable of stimulating tyrosine kinase activity, identifying whether an albumin fusion protein of the present invention or a molecule induced by a fusion protein of the present invention is capable of activating tyrosine kinase signal transduction pathways is of interest. Therefore, the following protocol is designed to identify such molecules capable of activating the tyrosine kinase signal transduction pathways.

[1081] Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4 degree C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

[1082] To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or a different concentrations of an albumin fusion protein of the invention, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na₃VO₄, 2 mM Na₄P₂O₇ and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN)) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4 degree C at 16,000 x g.

[1083] Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

[1084] Generally, the tyrosine kinase activity of an albumin fusion protein of the invention is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

[1085] The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂⁺ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30 degree C for 2 min. Initiate the reaction by adding 10ul of the control enzyme or the filtered supernatant.

[1086] The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

[1087] Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37 degree C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37 degree C for one hour. Wash the well as above.

[1088] Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

EXAMPLE 32: Assay Identifying Phosphorylation Activity.

[1089] As a potential alternative and/or complement to the assay of protein tyrosine kinase activity described in Example 31, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

[1090] Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4 degree C until use.

[1091] A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or varying concentrations of the fusion protein of the invention for 5-20 minutes. The cells are then solubilized and extracts filtered

directly into the assay plate.

[1092] After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation by the fusion protein of the present invention or a molecule induced by an albumin fusion protein of the present invention.

EXAMPLE 33: Phosphorylation Assay.

[1093] In order to assay for phosphorylation activity of an albumin fusion protein of the invention, a phosphorylation assay as described in U.S. Patent 5,958,405 (which is herein incorporated by reference) is utilized. Briefly, phosphorylation activity may be measured by phosphorylation of a protein substrate using gamma-labeled ^{32}P -ATP and quantitation of the incorporated radioactivity using a gamma radioisotope counter. The fusion protein of the invention is incubated with the protein substrate, ^{32}P -ATP, and a kinase buffer. The ^{32}P incorporated into the substrate is then separated from free ^{32}P -ATP by electrophoresis, and the incorporated ^{32}P is counted and compared to a negative control. Radioactivity counts above the negative control are indicative of phosphorylation activity of the fusion protein.

EXAMPLE 34: Detection of Phosphorylation Activity (Activation) of an Albumin Fusion Protein of the Invention in the Presence of Polypeptide Ligands.

[1094] Methods known in the art or described herein may be used to determine the phosphorylation activity of an albumin fusion protein of the invention. A preferred method of determining phosphorylation activity is by the use of the tyrosine phosphorylation assay as described in US 5,817,471 (incorporated herein by reference).

EXAMPLE 35: Assay for the Stimulation of Bone Marrow CD34+ Cell Proliferation.

[1095] This assay is based on the ability of human CD34+ to proliferate in the

presence of hematopoietic growth factors and evaluates the ability of fusion proteins of the invention to stimulate proliferation of CD34+ cells.

[1096] It has been previously shown that most mature precursors will respond to only a single signal. More immature precursors require at least two signals to respond. Therefore, to test the effect of fusion proteins of the invention on hematopoietic activity of a wide range of progenitor cells, the assay contains a given fusion protein of the invention in the presence or absence of hematopoietic growth factors. Isolated cells are cultured for 5 days in the presence of Stem Cell Factor (SCF) in combination with tested sample. SCF alone has a very limited effect on the proliferation of bone marrow (BM) cells, acting in such conditions only as a "survival" factor. However, combined with any factor exhibiting stimulatory effect on these cells (e.g., IL-3), SCF will cause a synergistic effect. Therefore, if the tested fusion protein has a stimulatory effect on hematopoietic progenitors, such activity can be easily detected. Since normal BM cells have a low level of cycling cells, it is likely that any inhibitory effect of a given fusion protein might not be detected. Accordingly, assays for an inhibitory effect on progenitors is preferably tested in cells that are first subjected to *in vitro* stimulation with SCF+IL-3, and then contacted with the compound that is being evaluated for inhibition of such induced proliferation.

[1097] Briefly, CD34+ cells are isolated using methods known in the art. The cells are thawed and resuspended in medium (QBSF 60 serum-free medium with 1% L-glutamine (500ml) Quality Biological, Inc., Gaithersburg, MD Cat# 160-204-101). After several gentle centrifugation steps at 200 x g, cells are allowed to rest for one hour. The cell count is adjusted to 2.5×10^5 cells/ml. During this time, 100 μ l of sterile water is added to the peripheral wells of a 96-well plate. The cytokines that can be tested with an albumin fusion protein of the invention in this assay is rhSCF (R&D Systems, Minneapolis, MN, Cat# 255-SC) at 50 ng/ml alone and in combination with rhSCF and rhIL-3 (R&D Systems, Minneapolis, MN, Cat# 203-ML) at 30 ng/ml. After one hour, 10 μ l of prepared cytokines, varying concentrations of an albumin fusion protein of the invention, and 20 μ l of diluted cells are added to the media which is already present in the wells to allow for a final total volume of 100 μ l. The plates are then placed in a 37°C/5% CO₂ incubator for five days.

[1098] Eighteen hours before the assay is harvested, 0.5 μ Ci/well of [3H] Thymidine is added in a 10 μ l volume to each well to determine the proliferation rate. The experiment is

terminated by harvesting the cells from each 96-well plate to a filtermat using the Tomtec Harvester 96. After harvesting, the filtermats are dried, trimmed and placed into OmniFilter assemblies consisting of one OmniFilter plate and one OmniFilter Tray. 60 μ l Microscint is added to each well and the plate sealed with TopSeal-A press-on sealing film. A bar code 15 sticker is affixed to the first plate for counting. The sealed plates are then loaded and the level of radioactivity determined via the Packard Top Count and the printed data collected for analysis. The level of radioactivity reflects the amount of cell proliferation.

[1099] The studies described in this example test the activity of a given fusion protein to stimulate bone marrow CD34+ cell proliferation. One skilled in the art could easily modify the exemplified studies to test the activity of fusion proteins and polynucleotides of the invention (e.g., gene therapy) as well as agonists and antagonists thereof. The ability of an albumin fusion protein of the invention to stimulate the proliferation of bone marrow CD34+ cells indicates that the albumin fusion protein and/or polynucleotides corresponding to the fusion protein are useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein.

EXAMPLE 36: Assay for Extracellular Matrix Enhanced Cell Response (EMECCR).

[1100] The objective of the Extracellular Matrix Enhanced Cell Response (EMECCR) assay is to evaluate the ability of fusion proteins of the invention to act on hematopoietic stem cells in the context of the extracellular matrix (ECM) induced signal.

[1101] Cells respond to the regulatory factors in the context of signal(s) received from the surrounding microenvironment. For example, fibroblasts, and endothelial and epithelial stem cells fail to replicate in the absence of signals from the ECM. Hematopoietic stem cells can undergo self-renewal in the bone marrow, but not in *in vitro* suspension culture. The ability of stem cells to undergo self-renewal *in vitro* is dependent upon their interaction with the stromal cells and the ECM protein fibronectin (fn). Adhesion of cells to fn is mediated by the $\alpha_5\beta_1$ and $\alpha_4\beta_1$ integrin receptors, which are expressed by human and mouse hematopoietic stem cells. The factor(s) which integrate with the ECM environment and are responsible for stimulating stem cell self-renewal have not yet been identified. Discovery of such factors should be of great interest in gene therapy and bone marrow transplant applications.

[1102] Briefly, polystyrene, non tissue culture treated, 96-well plates are coated with fn fragment at a coating concentration of $0.2 \mu\text{g}/\text{cm}^2$. Mouse bone marrow cells are plated (1,000 cells/well) in 0.2 ml of serum-free medium. Cells cultured in the presence of IL-3 (5 ng/ml) + SCF (50 ng/ml) would serve as the positive control, conditions under which little self-renewal but pronounced differentiation of the stem cells is to be expected. Albumin fusion proteins of the invention are tested with appropriate negative controls in the presence and absence of SCF(5.0 ng/ml), where volume of the administered composition containing the albumin fusion protein of the invention represents 10% of the total assay volume. The plated cells are then allowed to grow by incubating in a low oxygen environment (5% CO_2 , 7% O_2 , and 88% N_2) tissue culture incubator for 7 days. The number of proliferating cells within the wells is then quantitated by measuring thymidine incorporation into cellular DNA. Verification of the positive hits in the assay will require phenotypic characterization of the cells, which can be accomplished by scaling up of the culture system and using appropriate antibody reagents against cell surface antigens and FACScan.

[1103] If a particular fusion protein of the present invention is found to be a stimulator of hematopoietic progenitors, the fusion protein and polynucleotides corresponding to the fusion protein may be useful for example, in the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein. The fusion protein may also be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

[1104] Additionally, the albumin fusion proteins of the invention and polynucleotides encoding albumin fusion proteins of the invention, may also be employed to inhibit the proliferation and differentiation of hematopoietic cells and therefore may be employed to protect bone marrow stem cells from chemotherapeutic agents during chemotherapy. This antiproliferative effect may allow administration of higher doses of chemotherapeutic agents and, therefore, more effective chemotherapeutic treatment.

[1105] Moreover, fusion proteins of the invention and polynucleotides encoding albumin fusion proteins of the invention may also be useful for the treatment and diagnosis of hematopoietic related disorders such as, anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia, since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex-vivo culture, bone marrow transplantation,

bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

EXAMPLE 37: Human Dermal Fibroblast and Aortic Smooth Muscle Cell Proliferation.

[1106] An albumin fusion protein of the invention is added to cultures of normal human dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AoSMC) and two co-assays are performed with each sample. The first assay examines the effect of the fusion protein on the proliferation of normal human dermal fibroblasts (NHDF) or aortic smooth muscle cells (AoSMC). Aberrant growth of fibroblasts or smooth muscle cells is a part of several pathological processes, including fibrosis, and restenosis. The second assay examines IL6 production by both NHDF and SMC. IL6 production is an indication of functional activation. Activated cells will have increased production of a number of cytokines and other factors, which can result in a proinflammatory or immunomodulatory outcome. Assays are run with and without co-TNF α stimulation, in order to check for costimulatory or inhibitory activity.

[1107] Briefly, on day 1, 96-well black plates are set up with 1000 cells/well (NHDF) or 2000 cells/well (AoSMC) in 100 μ l culture media. NHDF culture media contains: Clonetics FB basal media, 1mg/ml hFGF, 5mg/ml insulin, 50mg/ml gentamycin, 2%FBS, while AoSMC culture media contains Clonetics SM basal media, 0.5 μ g/ml hEGF, 5mg/ml insulin, 1 μ g/ml hFGF, 50mg/ml gentamycin, 50 μ g/ml Amphotericin B, 5%FBS. After incubation at 37°C for at least 4-5 hours culture media is aspirated and replaced with growth arrest media. Growth arrest media for NHDF contains fibroblast basal media, 50mg/ml gentamycin, 2% FBS, while growth arrest media for AoSMC contains SM basal media, 50mg/ml gentamycin, 50 μ g/ml Amphotericin B, 0.4% FBS. Incubate at 37 °C until day 2.

[1108] On day 2, serial dilutions and templates of an albumin fusion protein of the invention are designed such that they always include media controls and known-protein controls. For both stimulation and inhibition experiments, proteins are diluted in growth arrest media. For inhibition experiments, TNF α is added to a final concentration of 2ng/ml (NHDF) or 5ng/ml (AoSMC). Add 1/3 vol media containing controls or an albumin fusion protein of the invention and incubate at 37 degrees C/5% CO $_2$ until day 5.

[1109] Transfer 60 μ l from each well to another labeled 96-well plate, cover with a plate-sealer, and store at 4 degrees C until Day 6 (for IL6 ELISA). To the remaining 100 μ l

in the cell culture plate, aseptically add Alamar Blue in an amount equal to 10% of the culture volume (10 μ l). Return plates to incubator for 3 to 4 hours. Then measure fluorescence with excitation at 530nm and emission at 590nm using the CytoFluor. This yields the growth stimulation/inhibition data.

[1110] On day 5, the IL6 ELISA is performed by coating a 96 well plate with 50-100 μ l/well of Anti-Human IL6 Monoclonal antibody diluted in PBS, pH 7.4, incubate ON at room temperature.

[1111] On day 6, empty the plates into the sink and blot on paper towels. Prepare Assay Buffer containing PBS with 4% BSA. Block the plates with 200 μ l/well of Pierce Super Block blocking buffer in PBS for 1-2 hr and then wash plates with wash buffer (PBS, 0.05% Tween-20). Blot plates on paper towels. Then add 50 μ l/well of diluted Anti-Human IL-6 Monoclonal, Biotin-labeled antibody at 0.50 mg/ml. Make dilutions of IL-6 stock in media (30, 10, 3, 1, 0.3, 0 ng/ml). Add duplicate samples to top row of plate. Cover the plates and incubate for 2 hours at RT on shaker.

[1112] Plates are washed with wash buffer and blotted on paper towels. Dilute EU-labeled Streptavidin 1:1000 in Assay buffer, and add 100 μ l/well. Cover the plate and incubate 1 h at RT. Plates are again washed with wash buffer and blotted on paper towels.

[1113] Add 100 μ l/well of Enhancement Solution. Shake for 5 minutes. Read the plate on the Wallac DELFIA Fluorometer. Readings from triplicate samples in each assay were tabulated and averaged.

[1114] A positive result in this assay suggests AoSMC cell proliferation and that the albumin fusion protein may be involved in dermal fibroblast proliferation and/or smooth muscle cell proliferation. A positive result also suggests many potential uses of the fusion protein and polynucleotides encoding the albumin fusion protein. For example, inflammation and immune responses, wound healing, and angiogenesis, as detailed throughout this specification. Particularly, fusion proteins may be used in wound healing and dermal regeneration, as well as the promotion of vasculogenesis, both of the blood vessels and lymphatics. The growth of vessels can be used in the treatment of, for example, cardiovascular diseases. Additionally, fusion proteins showing antagonistic activity in this assay may be useful in treating diseases, disorders, and/or conditions which involve angiogenesis by acting as an anti-vascular agent (e.g., anti-angiogenesis). These diseases,

disorders, and/or conditions are known in the art and/or are described herein, such as, for example, malignancies, solid tumors, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophilic joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis. Moreover, albumin fusion proteins that act as antagonists in this assay may be useful in treating anti-hyperproliferative diseases and/or anti-inflammatory known in the art and/or described herein.

EXAMPLE 38: Cellular Adhesion Molecule (CAM) Expression on Endothelial Cells.

[1115] The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

[1116] Briefly, endothelial cells (e.g., Human Umbilical Vein Endothelial cells (HUVECs)) are grown in a standard 96 well plate to confluence, growth medium is removed from the cells and replaced with 100 μ l of 199 Medium (10% fetal bovine serum (FBS)). Samples for testing (containing an albumin fusion protein of the invention) and positive or negative controls are added to the plate in triplicate (in 10 μ l volumes). Plates are then incubated at 37°C for either 5 h (selectin and integrin expression) or 24 h (integrin expression

only). Plates are aspirated to remove medium and 100 μ l of 0.1% paraformaldehyde-PBS(with Ca^{++} and Mg^{++}) is added to each well. Plates are held at 4°C for 30 min. Fixative is removed from the wells and wells are washed 1X with PBS(+Ca,Mg) + 0.5% BSA and drained. 10 μ l of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 μ g/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed three times with PBS(+Ca,Mg) + 0.5% BSA. 20 μ l of diluted ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution, referred to herein as the working dilution) are added to each well and incubated at 37°C for 30 min. Wells are washed three times with PBS(+Ca,Mg)+0.5% BSA. Dissolve 1 tablet of p-Nitrophenol Phosphate pNPP per 5 ml of glycine buffer (pH 10.4). 100 μ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: 1:5,000 (10^0) > $10^{-0.5}$ > 10^{-1} > $10^{-1.5}$. 5 μ l of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 μ l of pNPP reagent is then added to each of the standard wells. The plate is incubated at 37°C for 4h. A volume of 50 μ l of 3M NaOH is added to all wells. The plate is read on a plate reader at 405 nm using the background subtraction option on blank wells filled with glycine buffer only. Additionally, the template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

EXAMPLE 39: Alamar Blue Endothelial Cells Proliferation Assay.

[1117] This assay may be used to quantitatively determine protein mediated inhibition of bFGF-induced proliferation of Bovine Lymphatic Endothelial Cells (LECs), Bovine Aortic Endothelial Cells (BAECs) or Human Microvascular Uterine Myometrial Cells (UTMECs). This assay incorporates a fluorometric growth indicator based on detection of metabolic activity. A standard Alamar Blue Proliferation Assay is prepared in EGM-2MV with 10 ng /ml of bFGF added as a source of endothelial cell stimulation. This assay may be used with a variety of endothelial cells with slight changes in growth medium and cell concentration. Dilutions of protein batches to be tested are diluted as appropriate. Serum-free medium (GIBCO SFM) without bFGF is used as a non-stimulated control and Angiostatin or TSP-1

are included as a known inhibitory controls.

[1118] Briefly, LEC, BAECs or UTMECs are seeded in growth media at a density of 5000 to 2000 cells/well in a 96 well plate and placed at 37 degreesC overnight. After the overnight incubation of the cells, the growth media is removed and replaced with GIBCO EC-SFM. The cells are treated with the appropriate dilutions of an albumin fusion protein of the invention or control protein sample(s) (prepared in SFM) in triplicate wells with additional bFGF to a concentration of 10 ng/ ml. Once the cells have been treated with the samples, the plate(s) is/are placed back in the 37° C incubator for three days. After three days 10 ml of stock alamar blue (Biosource Cat# DAL1100) is added to each well and the plate(s) is/are placed back in the 37°C incubator for four hours. The plate(s) are then read at 530nm excitation and 590nm emission using the CytoFluor fluorescence reader. Direct output is recorded in relative fluorescence units.

[1119] Alamar blue is an oxidation-reduction indicator that both fluoresces and changes color in response to chemical reduction of growth medium resulting from cell growth. As cells grow in culture, innate metabolic activity results in a chemical reduction of the immediate surrounding environment. Reduction related to growth causes the indicator to change from oxidized (non-fluorescent blue) form to reduced (fluorescent red) form (i.e., stimulated proliferation will produce a stronger signal and inhibited proliferation will produce a weaker signal and the total signal is proportional to the total number of cells as well as their metabolic activity). The background level of activity is observed with the starvation medium alone. This is compared to the output observed from the positive control samples (bFGF in growth medium) and protein dilutions.

EXAMPLE 40: Detection of Inhibition of a Mixed Lymphocyte Reaction.

[1120] This assay can be used to detect and evaluate inhibition of a Mixed Lymphocyte Reaction (MLR) by fusion proteins of the invention. Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by the albumin fusion proteins that inhibit MLR since the peripheral blood mononuclear fraction used in this assay includes T, B and natural killer lymphocytes, as well as monocytes and dendritic cells.

[1121] Albumin fusion proteins of the invention found to inhibit the MLR may find application in diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

[1122] Briefly, PBMCs from human donors are purified by density gradient centrifugation using Lymphocyte Separation Medium (LSM[®], density 1.0770 g/ml, Organon Teknika Corporation, West Chester, PA). PBMCs from two donors are adjusted to 2×10^6 cells/ml in RPMI-1640 (Life Technologies, Grand Island, NY) supplemented with 10% FCS and 2 mM glutamine. PBMCs from a third donor is adjusted to 2×10^5 cells/ml. Fifty microliters of PBMCs from each donor is added to wells of a 96-well round bottom microtiter plate. Dilutions of the fusion protein test material (50 μ l) is added in triplicate to microtiter wells. Test samples (of the protein of interest) are added for final dilution of 1:4; rhuIL-2 (R&D Systems, Minneapolis, MN, catalog number 202-IL) is added to a final concentration of 1 μ g/ml; anti-CD4 mAb (R&D Systems, clone 34930.11, catalog number MAB379) is added to a final concentration of 10 μ g/ml. Cells are cultured for 7-8 days at 37°C in 5% CO₂, and 1 μ C of [³H] thymidine is added to wells for the last 16 hrs of culture. Cells are harvested and thymidine incorporation determined using a Packard TopCount. Data is expressed as the mean and standard deviation of triplicate determinations.

[1123] Samples of the fusion protein of interest are screened in separate experiments and compared to the negative control treatment, anti-CD4 mAb, which inhibits proliferation of lymphocytes and the positive control treatment, IL-2 (either as recombinant material or supernatant), which enhances proliferation of lymphocytes.

EXAMPLE 41: Assays for Protease Activity.

[1124] The following assay may be used to assess protease activity of an albumin fusion protein of the invention.

[1125] Gelatin and casein zymography are performed essentially as described (Heusen et al., *Anal. Biochem.*, 102:196-202 (1980); Wilson et al., *Journal of Urology*, 149:653-658

(1993)). Samples are run on 10% polyacryamide/0.1% SDS gels containing 1% gelatin or casein, soaked in 2.5% triton at room temperature for 1 hour, and in 0.1M glycine, pH 8.3 at 37°C 5 to 16 hours. After staining in amido black areas of proteolysis appear as clear areas against the blue-black background. Trypsin (Sigma T8642) is used as a positive control.

[1126] Protease activity is also determined by monitoring the cleavage of n-a-benzoyl-L-arginine ethyl ester (BAEE) (Sigma B-4500. Reactions are set up in (25mMNaPO₄, 1mM EDTA, and 1mM BAEE), pH 7.5. Samples are added and the change in adsorbance at 260nm is monitored on the Beckman DU-6 spectrophotometer in the time-drive mode. Trypsin is used as a positive control.

[1127] Additional assays based upon the release of acid-soluble peptides from casein or hemoglobin measured as adsorbance at 280 nm or colorimetrically using the Folin method are performed as described in Bergmeyer, et al., *Methods of Enzymatic Analysis*, 5 (1984). Other assays involve the solubilization of chromogenic substrates (Ward, *Applied Science*, 251-317 (1983)).

EXAMPLE 42: Identifying Serine Protease Substrate Specificity.

[1128] Methods known in the art or described herein may be used to determine the substrate specificity of the albumin fusion proteins of the present invention having serine protease activity. A preferred method of determining substrate specificity is by the use of positional scanning synthetic combinatorial libraries as described in GB 2 324 529 (incorporated herein in its entirety).

EXAMPLE 43: Ligand Binding Assays.

[1129] The following assay may be used to assess ligand binding activity of an albumin fusion protein of the invention.

[1130] Ligand binding assays provide a direct method for ascertaining receptor pharmacology and are adaptable to a high throughput format. The purified ligand for an albumin fusion protein of the invention is radiolabeled to high specific activity (50-2000 Ci/mmol) for binding studies. A determination is then made that the process of radiolabeling does not diminish the activity of the ligand towards the fusion protein. Assay conditions for buffers, ions, pH and other modulators such as nucleotides are optimized to establish a workable signal to noise ratio for both membrane and whole cell polypeptide sources. For

these assays, specific polypeptide binding is defined as total associated radioactivity minus the radioactivity measured in the presence of an excess of unlabeled competing ligand. Where possible, more than one competing ligand is used to define residual nonspecific binding.

EXAMPLE 44: Functional Assay in *Xenopus* Oocytes.

[1131] Capped RNA transcripts from linearized plasmid templates encoding an albumin fusion protein of the invention is synthesized in vitro with RNA polymerases in accordance with standard procedures. In vitro transcripts are suspended in water at a final concentration of 0.2 mg/ml. Ovarian lobes are removed from adult female toads, Stage V defolliculated oocytes are obtained, and RNA transcripts (10 ng/oocyte) are injected in a 50 nl bolus using a microinjection apparatus. Two electrode voltage clamps are used to measure the currents from individual *Xenopus oocytes* in response fusion protein and polypeptide agonist exposure. Recordings are made in Ca²⁺ free Barth's medium at room temperature. The *Xenopus* system can be used to screen known ligands and tissue/cell extracts for activating ligands.

EXAMPLE 45: Microphysiometric Assays.

[1132] Activation of a wide variety of secondary messenger systems results in extrusion of small amounts of acid from a cell. The acid formed is largely as a result of the increased metabolic activity required to fuel the intracellular signaling process. The pH changes in the media surrounding the cell are very small but are detectable by the CYTOSENSOR microphysiometer (Molecular Devices Ltd., Menlo Park, Calif.). The CYTOSENSOR is thus capable of detecting the ability of an albumin fusion protein of the invention to activate secondary messengers that are coupled to an energy utilizing intracellular signaling pathway.

EXAMPLE 46: Extract/Cell Supernatant Screening.

[1133] A large number of mammalian receptors exist for which there remains, as yet, no cognate activating ligand (agonist). Thus, active ligands for these receptors may not be included within the ligands banks as identified to date. Accordingly, the albumin fusion proteins of the invention can also be functionally screened (using calcium, cAMP, microphysiometer, oocyte electrophysiology, etc., functional screens) against tissue extracts

to identify natural ligands for the Therapeutic protein portion and/or albumin protein portion of an albumin fusion protein of the invention. Extracts that produce positive functional responses can be sequentially subfractionated until an activating ligand is isolated and identified.

EXAMPLE 47: ATP-binding assay.

[1134] The following assay may be used to assess ATP-binding activity of fusion proteins of the invention.

[1135] ATP-binding activity of an albumin fusion protein of the invention may be detected using the ATP-binding assay described in U.S. Patent 5,858,719, which is herein incorporated by reference in its entirety. Briefly, ATP-binding to an albumin fusion protein of the invention is measured via photoaffinity labeling with 8-azido-ATP in a competition assay. Reaction mixtures containing 1 mg/ml of ABC transport protein are incubated with varying concentrations of ATP, or the non-hydrolyzable ATP analog adenylyl-5'-imidodiphosphate for 10 minutes at 4°C. A mixture of 8-azido-ATP (Sigma Chem. Corp., St. Louis, MO.) plus 8-azido-ATP (³²P-ATP) (5 mCi/μmol, ICN, Irvine CA.) is added to a final concentration of 100 μM and 0.5 ml aliquots are placed in the wells of a porcelain spot plate on ice. The plate is irradiated using a short wave 254 nm UV lamp at a distance of 2.5 cm from the plate for two one-minute intervals with a one-minute cooling interval in between. The reaction is stopped by addition of dithiothreitol to a final concentration of 2mM. The incubations are subjected to SDS-PAGE electrophoresis, dried, and autoradiographed. Protein bands corresponding to the albumin fusion proteins of the invention are excised, and the radioactivity quantified. A decrease in radioactivity with increasing ATP or adenylyl-5'-imidodiphosphate provides a measure of ATP affinity to the fusion protein.

EXAMPLE 48: Identification Of Signal Transduction Proteins That Interact With An albumin fusion protein Of The Present Invention.

[1136] Albumin fusion proteins of the invention may serve as research tools for the identification, characterization and purification of signal transduction pathway proteins or receptor proteins. Briefly, a labeled fusion protein of the invention is useful as a reagent for the purification of molecules with which it interacts. In one embodiment of affinity

purification, an albumin fusion protein of the invention is covalently coupled to a chromatography column. Cell-free extract derived from putative target cells, such as carcinoma tissues, is passed over the column, and molecules with appropriate affinity bind to the albumin fusion protein. The protein complex is recovered from the column, dissociated, and the recovered molecule subjected to N-terminal protein sequencing. This amino acid sequence is then used to identify the captured molecule or to design degenerate oligonucleotide probes for cloning the relevant gene from an appropriate cDNA library.

EXAMPLE 49: IL-6 Bioassay.

[1137] A variety of assays are known in the art for testing the proliferative effects of an albumin fusion protein of the invention. For example, one such assay is the IL-6 Bioassay as described by Marz *et al.* (*Proc. Natl. Acad. Sci., U.S.A.*, 95:3251-56 (1998), which is herein incorporated by reference). After 68 hrs. at 37°C, the number of viable cells is measured by adding the tetrazolium salt thiazolyl blue (MTT) and incubating for a further 4 hrs. at 37°C. B9 cells are lysed by SDS and optical density is measured at 570 nm. Controls containing IL-6 (positive) and no cytokine (negative) are Briefly, IL-6 dependent B9 murine cells are washed three times in IL-6 free medium and plated at a concentration of 5,000 cells per well in 50 µl, and 50 µl of fusion protein of the invention is added. Enhanced proliferation in the test sample(s) (containing an albumin fusion protein of the invention) relative to the negative control is indicative of proliferative effects mediated by the fusion protein.

EXAMPLE 50: Support of Chicken Embryo Neuron Survival.

[1138] To test whether sympathetic neuronal cell viability is supported by an albumin fusion protein of the invention, the chicken embryo neuronal survival assay of Senaldi *et al* may be utilized (*Proc. Natl. Acad. Sci., U.S.A.*, 96:11458-63 (1998), which is herein incorporated by reference). Briefly, motor and sympathetic neurons are isolated from chicken embryos, resuspended in L15 medium (with 10% FCS, glucose, sodium selenite, progesterone, conalbumin, putrescine, and insulin; Life Technologies, Rockville, MD.) and Dulbecco's modified Eagles medium [with 10% FCS, glutamine, penicillin, and 25 mM Hepes buffer (pH 7.2); Life Technologies, Rockville, MD.], respectively, and incubated at 37°C in 5% CO₂ in the presence of different concentrations of the purified fusion protein of

the invention, as well as a negative control lacking any cytokine. After 3 days, neuron survival is determined by evaluation of cellular morphology, and through the use of the colorimetric assay of Mosmann (Mosmann, T., *J. Immunol. Methods*, 65:55-63 (1983)). Enhanced neuronal cell viability as compared to the controls lacking cytokine is indicative of the ability of the albumin fusion protein to enhance the survival of neuronal cells.

EXAMPLE 51: Assay for Phosphatase Activity.

[1139] The following assay may be used to assess serine/threonine phosphatase (PTPase) activity of an albumin fusion protein of the invention.

[1140] In order to assay for serine/threonine phosphatase (PTPase) activity, assays can be utilized which are widely known to those skilled in the art. For example, the serine/threonine phosphatase (PSPase) activity of an albumin fusion protein of the invention may be measured using a PSPase assay kit from New England Biolabs, Inc. Myelin basic protein (MyBP), a substrate for PSPase, is phosphorylated on serine and threonine residues with cAMP-dependent Protein Kinase in the presence of [³²P]ATP. Protein serine/threonine phosphatase activity is then determined by measuring the release of inorganic phosphate from ³²P-labeled MyBP.

EXAMPLE 52: Interaction of Serine/Threonine Phosphatases with other Proteins.

[1141] Fusion proteins of the invention having serine/threonine phosphatase activity (e.g., as determined in Example 51) are useful, for example, as research tools for the identification, characterization and purification of additional interacting proteins or receptor proteins, or other signal transduction pathway proteins. Briefly, a labeled fusion protein of the invention is useful as a reagent for the purification of molecules with which it interacts. In one embodiment of affinity purification, an albumin fusion protein of the invention is covalently coupled to a chromatography column. Cell-free extract derived from putative target cells, such as neural or liver cells, is passed over the column, and molecules with appropriate affinity bind to the fusion protein. The fusion protein -complex is recovered from the column, dissociated, and the recovered molecule subjected to N-terminal protein sequencing. This amino acid sequence is then used to identify the captured molecule or to design degenerate oligonucleotide probes for cloning the relevant gene from an appropriate cDNA library.

EXAMPLE 53: Assaying for Heparanase Activity.

[1142] There are numerous assays known in the art that may be employed to assay for heparanase activity of an albumin fusion protein of the invention. In one example, heparanase activity of an albumin fusion protein of the invention, is assayed as described by Vlodavsky et al., (Vlodavsky et al., Nat. Med., 5:793-802 (1999)). Briefly, cell lysates, conditioned media, intact cells (1×10^6 cells per 35-mm dish), cell culture supernatant, or purified fusion protein are incubated for 18 hrs at 37°C, pH 6.2-6.6, with ^{35}S -labeled ECM or soluble ECM derived peak I proteoglycans. The incubation medium is centrifuged and the supernatant is analyzed by gel filtration on a Sepharose CL-6B column (0.9 x 30 cm). Fractions are eluted with PBS and their radioactivity is measured. Degradation fragments of heparan sulfate side chains are eluted from Sepharose 6B at $0.5 < K_{av} < 0.8$ (peak II). Each experiment is done at least three times. Degradation fragments corresponding to "peak II," as described by Vlodavsky et al., is indicative of the activity of an albumin fusion protein of the invention in cleaving heparan sulfate.

EXAMPLE 54: Immobilization of biomolecules.

[1143] This example provides a method for the stabilization of an albumin fusion protein of the invention in non-host cell lipid bilayer constructs (see, e.g., Bieri et al., Nature Biotech 17:1105-1108 (1999), hereby incorporated by reference in its entirety herein) which can be adapted for the study of fusion proteins of the invention in the various functional assays described above. Briefly, carbohydrate-specific chemistry for biotinylation is used to confine a biotin tag to an albumin fusion protein of the invention, thus allowing uniform orientation upon immobilization. A 50uM solution of an albumin fusion protein of the invention in washed membranes is incubated with 20 mM NaIO₄ and 1.5 mg/ml (4mM) BACH or 2 mg/ml (7.5mM) biotin-hydrazide for 1 hr at room temperature (reaction volume, 150ul). Then the sample is dialyzed (Pierce Slidealizer Cassett, 10 kDa cutoff; Pierce Chemical Co., Rockford IL) at 4°C first for 5 h, exchanging the buffer after each hour, and finally for 12 h against 500 ml buffer R (0.15 M NaCl, 1 mM MgCl₂, 10 mM sodium phosphate, pH7). Just before addition into a cuvette, the sample is diluted 1:5 in buffer ROG50 (Buffer R supplemented with 50 mM octylglucoside).

EXAMPLE 55: Assays for Metalloproteinase Activity.

[1144] Metalloproteinases are peptide hydrolases which use metal ions, such as Zn^{2+} , as the catalytic mechanism. Metalloproteinase activity of an albumin fusion protein of the present invention can be assayed according to methods known in the art. The following exemplary methods are provided:

Proteolysis of alpha-2-macroglobulin

[1145] To confirm protease activity, a purified fusion protein of the invention is mixed with the substrate alpha-2-macroglobulin (0.2 unit/ml; Boehringer Mannheim, Germany) in 1x assay buffer (50 mM HEPES, pH 7.5, 0.2 M NaCl, 10 mM CaCl_2 , 25 μM ZnCl_2 and 0.05% Brij-35) and incubated at 37°C for 1-5 days. Trypsin is used as positive control. Negative controls contain only alpha-2-macroglobulin in assay buffer. The samples are collected and boiled in SDS-PAGE sample buffer containing 5% 2-mercaptoethanol for 5-min, then loaded onto 8% SDS-polyacrylamide gel. After electrophoresis the proteins are visualized by silver staining. Proteolysis is evident by the appearance of lower molecular weight bands as compared to the negative control.

Inhibition of alpha-2-macroglobulin proteolysis by inhibitors of metalloproteinases

[1146] Known metalloproteinase inhibitors (metal chelators (EDTA, EGTA, AND HgCl_2), peptide metalloproteinase inhibitors (TIMP-1 and TIMP-2), and commercial small molecule MMP inhibitors) may also be used to characterize the proteolytic activity of an albumin fusion protein of the invention. Three synthetic MMP inhibitors that may be used are: MMP inhibitor I, [IC_{50} = 1.0 μM against MMP-1 and MMP-8; IC_{50} = 30 μM against MMP-9; IC_{50} = 150 μM against MMP-3]; MMP-3 (stromelysin-1) inhibitor I [IC_{50} = 5 μM against MMP-3], and MMP-3 inhibitor II [K_i = 130 nM against MMP-3]; inhibitors available through Calbiochem, catalog # 444250, 444218, and 444225, respectively). Briefly, different concentrations of the small molecule MMP inhibitors are mixed with a purified fusion protein of the invention (50 $\mu\text{g/ml}$) in 22.9 μl of 1x HEPES buffer (50 mM HEPES, pH 7.5, 0.2 M NaCl, 10 mM CaCl_2 , 25 μM ZnCl_2 and 0.05%Brij-35) and incubated at room temperature (24 °C) for 2-hr, then 7.1 μl of substrate alpha-2-macroglobulin (0.2 unit/ml) is added and incubated at 37°C for 20-hr. The reactions are stopped by adding 4x sample buffer and boiled immediately for 5 minutes. After SDS-PAGE, the protein bands are visualized by silver stain.

Synthetic Fluorogenic Peptide Substrates Cleavage Assay

[1147] The substrate specificity for fusion proteins of the invention with demonstrated metalloproteinase activity may be determined using techniques known in the art, such as using synthetic fluorogenic peptide substrates (purchased from BACHEM Bioscience Inc). Test substrates include, M-1985, M-2225, M-2105, M-2110, and M-2255. The first four are MMP substrates and the last one is a substrate of tumor necrosis factor- α (TNF- α) converting enzyme (TACE). These substrates are preferably prepared in 1:1 dimethyl sulfoxide (DMSO) and water. The stock solutions are 50-500 μ M. Fluorescent assays are performed by using a Perkin Elmer LS 50B luminescence spectrometer equipped with a constant temperature water bath. The excitation λ is 328 nm and the emission λ is 393 nm. Briefly, the assay is carried out by incubating 176 μ l 1x HEPES buffer (0.2 M NaCl, 10 mM CaCl₂, 0.05% Brij-35 and 50 mM HEPES, pH 7.5) with 4 μ l of substrate solution (50 μ M) at 25 °C for 15 minutes, and then adding 20 μ l of a purified fusion protein of the invention into the assay cuvette. The final concentration of substrate is 1 μ M. Initial hydrolysis rates are monitored for 30-min.

EXAMPLE 56: Occurrence of Diabetes in NOD Mice.

[1148] Female NOD (non-obese diabetic) mice are characterized by displaying IDDM with a course which is similar to that found in humans, although the disease is more pronounced in female than male NOD mice. Hereinafter, unless otherwise stated, the term "NOD mouse" refers to a female NOD mouse. NOD mice have a progressive destruction of beta cells which is caused by a chronic autoimmune disease. Thus, NOD mice begin life with euglycemia, or normal blood glucose levels. By about 15 to 16 weeks of age, however, NOD mice start becoming hyperglycemic, indicating the destruction of the majority of their pancreatic beta cells and the corresponding inability of the pancreas to produce sufficient insulin. Thus, both the cause and the progression of the disease are similar to human IDDM patients.

[1149] *In vivo* assays of efficacy of the immunization regimens can be assessed in female NOD/LtJ mice (commercially available from The Jackson Laboratory, Bar Harbor, Me.). In the literature, it's reported that 80% of female mice develop diabetes by 24 weeks of

age and onset of insulinitis begins between 6-8 weeks age. NOD mice are inbred and highly responsive to a variety of immunoregulatory strategies. Adult NOD mice (6-8 weeks of age) have an average mass of 20-25 g.

[1150] These mice can be either untreated (control), treated with the therapeutics of the subject invention (e.g., albumin fusion proteins of the invention and fragments and variants thereof), alone or in combination with other therapeutic compounds stated above. The effect of these various treatments on the progression of diabetes can be measured as follows:

[1151] At 14 weeks of age, the female NOD mice can be phenotyped according to glucose tolerance. Glucose tolerance can be measured with the intraperitoneal glucose tolerance test (IPGTT). Briefly, blood is drawn from the paraorbital plexus at 0 minutes and 60 minutes after the intraperitoneal injection of glucose (1 g/kg body weight). Normal tolerance is defined as plasma glucose at 0 minutes of less than 144 mg %, or at 60 minutes of less than 160 mg %. Blood glucose levels are determined with a Glucometer Elite apparatus.

[1152] Based upon this phenotypic analysis, animals can be allocated to the different experimental groups. In particular, animals with more elevated blood glucose levels can be assigned to the impaired glucose tolerance group. The mice can be fed ad libitum and can be supplied with acidified water (pH 2.3).

[1153] The glucose tolerant and intolerant mice can be further subdivided into control, albumin fusion proteins of the subject invention, and albumin fusion proteins/therapeutic compounds combination groups. Mice in the control group can receive an interperitoneal injection of vehicle daily, six times per week. Mice in the albumin fusion group can receive an interperitoneal injection of the therapeutics of the subject invention (e.g., albumin fusion proteins of the invention and fragments and variants thereof) in vehicle daily, six times per week. Mice in the albumin fusion proteins/therapeutic compounds combination group can receive both albumin fusion proteins and combinations of therapeutic compounds as described above.

[1154] The level of urine glucose in the NOD mice can be determined on a bi-weekly basis using Labstix (Bayer Diagnostics, Hampshire, England). Weight and fluid intake can also be determined on a bi-weekly basis. The onset of diabetes is defined after the appearance of glucosuria on two consecutive determinations. After 10 weeks of treatment, an additional IPGTT can be performed and animals can be sacrificed the following day.

[1155] Over the 10 week course of treatment, control animals in both the glucose tolerant and glucose intolerant groups develop diabetes at a rate of 60% and 86%, respectively (see US patent No. 5,866,546, Gross et al.). Thus, high rates of diabetes occur even in NOD mice which are initially glucose tolerant if no intervention is made.

[1156] Results can be confirmed by the measurement of blood glucose levels in NOD mice, before and after treatment. Blood glucose levels are measured as described above in both glucose tolerant and intolerant mice in all groups described.

[1157] In an alternative embodiment, the therapeutics of the subject invention (e.g., specific fusions disclosed as SEQ ID NO:Y and fragments and variants thereof) can be quantified using spectrometric analysis and appropriate protein quantities can be resuspended prior to injection in 50 μ l phosphate buffered saline (PBS) per dose. Two injections, one week apart, can be administered subcutaneously under the dorsal skin of each mouse. Monitoring can be performed on two separate occasions prior to immunization and can be performed weekly throughout the treatment and continued thereafter. Urine can be tested for glucose every week (Keto-Diastix.RTM.; Miles Inc., Kankakee, Ill.) and glycosuric mice can be checked for serum glucose (ExacTech.RTM., MediSense, Inc., Waltham, Mass.). Diabetes is diagnosed when fasting glycemia is greater than 2.5g/L.

EXAMPLE 57: Histological Examination of NOD Mice.

[1158] Histological examination of tissue samples from NOD mice can demonstrate the ability of the compositions of the present invention, and/or a combination of the compositions of the present invention with other therapeutic agents for diabetes, to increase the relative concentration of beta cells in the pancreas. The experimental method is as follows:

[1159] The mice from Example 56 can be sacrificed at the end of the treatment period and tissue samples can be taken from the pancreas. The samples can be fixed in 10% formalin in 0.9% saline and embedded in wax. Two sets of 5 serial 5 μ m sections can be cut for immunolabelling at a cutting interval of 150 μ m. Sections can be immunolabelled for insulin (guinea pig anti-insulin antisera dilution 1:1000, ICN Thames U.K.) and glucagon (rabbit anti-pancreatic glucagon antisera dilution 1:2000) and detected with peroxidase conjugated anti-guinea pig (Dako, High Wycombe, U.K.) or peroxidase conjugated anti-rabbit antisera (dilution 1:50, Dako).

[1160] The composition of the present invention may or may not have as strong an effect on the visible mass of beta cells as it does on the clinical manifestations of diabetes in glucose tolerant and glucose intolerant animals.

EXAMPLE 58: *In vivo* Mouse Model of NIDDM.

[1161] Male C57BL/6J mice from Jackson Laboratory (Bar Harbor, ME) can be obtained at 3 weeks of age and fed on conventional chow or diets enriched in either fat (35.5% wt/wt; Bioserv, Frenchtown, NJ) or fructose (60% wt/wt; Harlan Teklad, Madison, WI). The regular chow is composed of 4.5% wt/wt fat, 23% wt/wt protein, 31.9% wt/wt starch, 3.7% wt/wt fructose, and 5.3% wt/wt fiber. The high-fat (lard) diet is composed of 35.5% wt/wt fat, 20% wt/wt protein, 36.4% wt/wt starch, 0.0% wt/wt fructose, and 0.1% wt/wt fiber. The high-fructose diet is composed of 5% wt/wt fat, 20% wt/wt protein, 0.0% wt/wt starch, 60% wt/wt fructose, and 9.4% wt/wt fiber. The mice may be housed no more than five per cage at 22° +/- 3°C temperature- and 50% +/- 20% humidity-controlled room with a 12-hour light (6 am to 6 pm)/dark cycle (Luo et al., 1998, *Metabolism* 47(6): 663-8, "Nongenetic mouse models of non-insulin-dependent diabetes mellitus"; Larsen et al., *Diabetes* 50(11): 2530-9 (2001), "Systemic administration of the long-acting GLP-1 derivative NN2211 induces lasting and reversible weight loss in both normal and obese rats"). After exposure to the respective diets for 3 weeks, mice can be injected intraperitoneally with either streptozotocin, "STZ" (Sigma, St. Louis, MO), at 100 mg/kg body weight or vehicle (0.05 mol/L citric acid, pH 4.5) and kept on the same diet for the next 4 weeks. Under nonfasting conditions, blood is obtained 1, 2, and 4 weeks post-STZ by nipping the distal part of the tail. Samples are used to measure nonfasting plasma glucose and insulin concentrations. Body weight and food intake are recorded weekly.

[1162] To directly determine the effect of the high-fat diet on the ability of insulin to stimulate glucose disposal, the experiments can be initiated on three groups of mice, fat-fed, chow-fed injected with vehicle, and fat-fed injected with STZ at the end of the 7-week period described above. Mice can be fasted for 4 hours before the experiments. In the first series of experiments, mice can be anesthetized with methoxyflurane (Pitman-Moor, Mundelein, IL) inhalation. Regular insulin (Sigma) can be injected intravenously ([IV] 0.1 U/kg body weight) through a tail vein, and blood can be collected 3, 6, 9, 12, and 15 minutes after the injection from a different tail vein. Plasma glucose concentrations can be determined on

these samples, and the half-life ($t_{1/2}$) of glucose disappearance from plasma can be calculated using WinNonlin (Scientific Consulting, Apex, NC), a pharmacokinetics/pharmacodynamics software program.

[1163] In the second series of experiments, mice can be anesthetized with intraperitoneal sodium pentobarbital (Sigma). The abdominal cavity is opened, and the main abdominal vein is exposed and catheterized with a 24-gauge IV catheter (Johnson-Johnson Medical, Arlington, TX). The catheter is secured to muscle tissue adjacent to the abdominal vein, cut on the bottom of the syringe connection, and hooked to a prefilled PE50 plastic tube, which in turn is connected to a syringe with infusion solution. The abdominal cavity is then sutured closed. With this approach, there would be no blockage of backflow of the blood from the lower part of the body. Mice can be infused continuously with glucose (24.1 mg/kg/min) and insulin (10 mU/kg/min) at an infusion volume of 10 μ L/min. Retro-orbital blood samples (70 μ L each) can be taken 90, 105, 120, and 135 minutes after the start of infusion for measurement of plasma glucose and insulin concentrations. The mean of these four samples is used to estimate steady-state plasma glucose (SSPG) and insulin (SSPI) concentrations for each animal.

[1164] Finally, experiments to evaluate the ability of the albumin fusion proteins, the therapeutic compositions of the instant application, either alone or in combination with any one or more of the therapeutic drugs listed for the treatment of diabetes mellitus, to decrease plasma glucose can be performed in the following two groups of "NIDDM" mice models that are STZ-injected: (1) fat-fed C57BL/6J, and (2) fructose-fed C57BL/6J. Plasma glucose concentrations of the mice for these studies may range from 255 to 555 mg/dL. Mice are randomly assigned to treatment with either vehicle, albumin fusion therapeutics of the present invention either alone or in combination with any one or more of the therapeutic drugs listed for the treatment of diabetes mellitus. A total of three doses can be administered. Tail vein blood samples can be taken for measurement of the plasma glucose concentration before the first dose and 3 hours after the final dose.

[1165] Plasma glucose concentrations can be determined using the Glucose Diagnostic Kit from Sigma (Sigma No. 315), an enzyme colorimetric assay. Plasma insulin levels can be determined using the Rat Insulin RIA Kit from Linco Research (#RI-13K; St. Charles, MO).

EXAMPLE 59: *In vitro* H4Ile -SEAP Reporter Assays Establishing Involvement in Insulin Action.

The Various H4Ile Reporters

[1166] H4Ile/rMEP-SEAP: The malic enzyme promoter isolated from rat (rMEP) contains a PPAR-gamma element which is in the insulin pathway. This reporter construct is stably transfected into the liver H4Ile cell-line.

[1167] H4Ile/SREBP-SEAP: The sterol regulatory element binding protein (SREBP-1c) is a transcription factor which acts on the promoters of a number of insulin-responsive genes, for example, fatty acid synthetase (FAS), and which regulates expression of key genes in fatty acid metabolism in fibroblasts, adipocytes, and hepatocytes. SREBP-1c, also known as the adipocyte determination and differentiation factor 1 (ADD-1), is considered as the primary mediator of insulin effects on gene expression in adipose cells. It's activity is modulated by the levels of insulin, sterols, and glucose. This reporter construct is stably transfected into the liver H4Ile cell-line.

[1168] H4Ile/FAS-SEAP: The fatty acid synthetase reporter constructs contain a minimal SREBP-responsive FAS promoter. This reporter construct is stably transfected into the liver H4Ile cell-line.

[1169] H4Ile/PEPCK-SEAP: The phosphoenolpyruvate carboxykinase (PEPCK) promoter is the primary site of hormonal regulation of PEPCK gene transcription modulating PEPCK activity. PEPCK catalyzes a committed and rate-limiting step in hepatic gluconeogenesis and must therefore be carefully controlled to maintain blood glucose levels within normal limits. This reporter construct is stably transfected into the liver H4Ile cell-line.

[1170] These reporter constructs can also be stably transfected into 3T3-L1 fibroblasts and L6 myoblasts. These stable cell-lines are then differentiated into 3T3-L1 adipocytes and L6 myotubes as previously described in Example 13. The differentiated cell-lines can then be used in the SEAP assay described below.

Growth and Assay Medium

[1171] The growth medium comprises 10% Fetal Bovine Serum (FBS), 10% Calf Serum, 1% NEAA, 1x penicillin/streptomycin, and 0.75 mg/mL G418 (for H4Ile/rFAS-SEAP and H4Ile/SREBP-SEAP) or 0.50 mg/mL G418 (for H4Ile/rMEP-SEAP). For H4Ile/PEPCK-SEAP, the growth medium consists of 10% FBS, 1% penicillin/streptomycin, 15 mM HEPES

buffered saline, and 0.50 mg/mL G418.

[1172] The assay medium consists of low glucose DMEM medium (Life Technologies), 1% NEAA, 1x penicillin/streptomycin for the H4IIe/rFAS-SEAP, H4IIe/SREBP-SEAP, H4IIe/rMEP-SEAP reporters. The assay medium for H4IIe/PEPCK-SEAP reporter consists of 0.1% FBS, 1% penicillin/streptomycin, and 15 mM HEPES buffered saline.

Method

[1173] The 96-well plates are seeded at 75,000 cells/well in 100 μ L/well of growth medium until cells in log growth phase become adherent. Cells are starved for 48 hours by replacing growth medium with assay medium, 200 μ L/well. (For H4IIe/PEPCK-SEAP cells, assay medium containing 0.5 μ M dexamethasone is added at 100 μ L/well and incubated for approximately 20 hours). The assay medium is replaced thereafter with 100 μ L/well of fresh assay medium, and a 50 μ L aliquot of cell supernatant obtained from transfected cell-lines expressing the therapeutics of the subject invention (e.g., albumin fusion proteins of the invention and fragments and variants thereof) is added to the well. Supernatants from empty vector transfected cell-lines are used as negative control. Addition of 10 nM and/or 100 nM insulin to the wells is used as positive control. After 48 hours of incubation, the conditioned media are harvested and SEAP activity measured (Phospha-Light System protocol, Tropix #BP2500). Briefly, samples are diluted 1:4 in dilution buffer and incubated at 65 °C for 30 minutes to inactivate the endogenous non-placental form of SEAP. An aliquot of 50 μ L of the diluted samples is mixed with 50 μ L of SEAP Assay Buffer which contains a mixture of inhibitors active against the non-placental SEAP isoenzymes and is incubated for another 5 minutes. An aliquot of 50 μ L of CSPD chemiluminescent substrate which is diluted 1:20 in Emerald luminescence enhancer is added to the mixture and incubated for 15-20 minutes. Plates are read in a Dynex plate luminometer.

EXAMPLE 60: Transgenic Animals.

[1174] The albumin fusion proteins of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e.g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a

specific embodiment, techniques described herein or otherwise known in the art, are used to express fusion proteins of the invention in humans, as part of a gene therapy protocol.

[1175] Any technique known in the art may be used to introduce the polynucleotides encoding the albumin fusion proteins of the invention into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e.g., Ulmer et al., Science 259:1745 (1993); introducing nucleic acid constructs into embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

[1176] Any technique known in the art may be used to produce transgenic clones containing polynucleotides encoding albumin fusion proteins of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

[1177] The present invention provides for transgenic animals that carry the polynucleotides encoding the albumin fusion proteins of the invention in all their cells, as well as animals which carry these polynucleotides in some, but not all their cells, *i.e.*, mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, *e.g.*, head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci. USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide encoding the fusion protein of

the invention be integrated into the chromosomal site of the endogenous gene corresponding to the Therapeutic protein portion or albumin portion of the fusion protein of the invention, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

[1178] Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the polynucleotide encoding the fusion protein of the invention has taken place. The level of mRNA expression of the polynucleotide encoding the fusion protein of the invention in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, *in situ* hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of fusion protein-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the fusion protein.

[1179] Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene (i.e., polynucleotide encoding an albumin fusion protein of the invention) on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of fusion proteins of the invention and the Therapeutic protein and/or albumin component of the fusion protein of the invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

EXAMPLE 61: Method of Treatment Using Gene Therapy-Ex Vivo.

[1180] One method of gene therapy transplants fibroblasts, which are capable of expressing an albumin fusion protein of the present invention, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37 degree C for approximately one week.

[1181] At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

[1182] pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

[1183] Polynucleotides encoding an albumin fusion protein of the invention can be generated using techniques known in the art amplified using PCR primers which correspond to the 5' and 3' end sequences and optionally having appropriate restriction sites and initiation/stop codons, if necessary. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101,

which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

[1184] The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

[1185] Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether the albumin fusion protein is produced.

[1186] The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

EXAMPLE 62: Method of Treatment Using Gene Therapy - *In Vivo*.

[1187] Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences encoding an albumin fusion protein of the invention into an animal. Polynucleotides encoding albumin fusion proteins of the present invention may be operatively linked to (i.e., associated with) a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata et al., Cardiovasc. Res. 35(3):470-479 (1997); Chao et al., Pharmacol. Res. 35(6):517-522 (1997); Wolff, Neuromuscul. Disord. 7(5):314-318 (1997);

Schwartz et al., *Gene Ther.* 3(5):405-411 (1996); Tsurumi et al., *Circulation* 94(12):3281-3290 (1996) (incorporated herein by reference).

[1188] The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

[1189] The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, polynucleotides encoding albumin fusion proteins of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) *Ann. NY Acad. Sci.* 772:126-139 and Abdallah B. et al. (1995) *Biol. Cell* 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

[1190] The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

[1191] The polynucleotide construct can be delivered to the interstitial space of tissues within an animal, including muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently

delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

[1192] For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

[1193] The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

[1194] Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

[1195] After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 μ m cross-section of the individual

quadriceps muscles is histochemically stained for protein expression. A time course for fusion protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be used to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

EXAMPLE 63: Biological Effects of Fusion Proteins of the Invention.

Astrocyte and Neuronal Assays.

[1196] Albumin fusion proteins of the invention can be tested for activity in promoting the survival, neurite outgrowth, or phenotypic differentiation of cortical neuronal cells and for inducing the proliferation of glial fibrillary acidic protein immunopositive cells, astrocytes. The selection of cortical cells for the bioassay is based on the prevalent expression of FGF-1 and FGF-2 in cortical structures and on the previously reported enhancement of cortical neuronal survival resulting from FGF-2 treatment. A thymidine incorporation assay, for example, can be used to elucidate an albumin fusion protein of the invention's activity on these cells.

[1197] Moreover, previous reports describing the biological effects of FGF-2 (basic FGF) on cortical or hippocampal neurons *in vitro* have demonstrated increases in both neuron survival and neurite outgrowth (Walicke et al., "Fibroblast growth factor promotes survival of dissociated hippocampal neurons and enhances neurite extension." *Proc. Natl. Acad. Sci. USA* 83:3012-3016. (1986), assay herein incorporated by reference in its entirety). However, reports from experiments done on PC-12 cells suggest that these two responses are not necessarily synonymous and may depend on not only which FGF is being tested but also on which receptor(s) are expressed on the target cells. Using the primary cortical neuronal culture paradigm, the ability of an albumin fusion protein of the invention to induce neurite outgrowth can be compared to the response achieved with FGF-2 using, for example, a thymidine incorporation assay.

Fibroblast and endothelial cell assays.

[1198] Human lung fibroblasts are obtained from Clonetics (San Diego, CA) and maintained in growth media from Clonetics. Dermal microvascular endothelial cells are obtained from Cell Applications (San Diego, CA). For proliferation assays, the human lung fibroblasts and dermal microvascular endothelial cells can be cultured at 5,000 cells/well in a 96-well plate for one day in growth medium. The cells are then incubated for one day in 0.1% BSA basal medium. After replacing the medium with fresh 0.1% BSA medium, the cells are incubated with the test fusion protein of the invention proteins for 3 days. Alamar Blue (Alamar Biosciences, Sacramento, CA) is added to each well to a final concentration of 10%. The cells are incubated for 4 hr. Cell viability is measured by reading in a CytoFluor fluorescence reader. For the PGE₂ assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or fusion protein of the invention with or without IL-1 α for 24 hours. The supernatants are collected and assayed for PGE₂ by EIA kit (Cayman, Ann Arbor, MI). For the IL-6 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or with or without an albumin fusion protein of the invention and/or IL-1 α for 24 hours. The supernatants are collected and assayed for IL-6 by ELISA kit (Endogen, Cambridge, MA).

[1199] Human lung fibroblasts are cultured with FGF-2 or an albumin fusion protein of the invention for 3 days in basal medium before the addition of Alamar Blue to assess effects on growth of the fibroblasts. FGF-2 should show a stimulation at 10 - 2500 ng/ml which can be used to compare stimulation with the fusion protein of the invention.

Cell proliferation based on [3H]thymidine incorporation

[1200] The following [3H]Thymidine incorporation assay can be used to measure the effect of a Therapeutic proteins, e.g., growth factor proteins, on the proliferation of cells such as fibroblast cells, epithelial cells or immature muscle cells.

[1201] Sub-confluent cultures are arrested in G1 phase by an 18 h incubation in serum-free medium. Therapeutic proteins are then added for 24 h and during the last 4 h, the cultures are labeled with [3H]thymidine, at a final concentration of 0.33 μ M (25 Ci/mmol,

Amersham, Arlington Heights, IL). The incorporated [3H]thymidine is precipitated with ice-cold 10% trichloroacetic acid for 24 h. Subsequently, the cells are rinsed sequentially with ice-cold 10% trichloroacetic acid and then with ice-cold water. Following lysis in 0.5 M NaOH, the lysates and PBS rinses (500 ml) are pooled, and the amount of radioactivity is measured.

Parkinson Models.

[1202] The loss of motor function in Parkinson's disease is attributed to a deficiency of striatal dopamine resulting from the degeneration of the nigrostriatal dopaminergic projection neurons. An animal model for Parkinson's that has been extensively characterized involves the systemic administration of 1-methyl-4 phenyl 1,2,3,6-tetrahydropyridine (MPTP). In the CNS, MPTP is taken-up by astrocytes and catabolized by monoamine oxidase B to 1-methyl-4-phenyl pyridine (MPP^+) and released. Subsequently, MPP^+ is actively accumulated in dopaminergic neurons by the high-affinity reuptake transporter for dopamine. MPP^+ is then concentrated in mitochondria by the electrochemical gradient and selectively inhibits nicotinamide adenine disphosphate: ubiquinone oxidoreductionase (complex I), thereby interfering with electron transport and eventually generating oxygen radicals.

[1203] It has been demonstrated in tissue culture paradigms that FGF-2 (basic FGF) has trophic activity towards nigral dopaminergic neurons (Ferrari et al., Dev. Biol. 1989). Recently, Dr. Unsicker's group has demonstrated that administering FGF-2 in gel foam implants in the striatum results in the near complete protection of nigral dopaminergic neurons from the toxicity associated with MPTP exposure (Otto and Unsicker, J. Neuroscience, 1990).

[1204] Based on the data with FGF-2, an albumin fusion protein of the invention can be evaluated to determine whether it has an action similar to that of FGF-2 in enhancing dopaminergic neuronal survival *in vitro* and it can also be tested *in vivo* for protection of dopaminergic neurons in the striatum from the damage associated with MPTP treatment. The potential effect of an albumin fusion protein of the invention is first examined *in vitro* in a dopaminergic neuronal cell culture paradigm. The cultures are prepared by dissecting the midbrain floor plate from gestation day 14 Wistar rat embryos. The tissue is dissociated with trypsin and seeded at a density of 200,000 cells/cm² on polyorthinine-laminin coated glass

coverslips. The cells are maintained in Dulbecco's Modified Eagle's medium and F12 medium containing hormonal supplements (N1). The cultures are fixed with paraformaldehyde after 8 days *in vitro* and are processed for tyrosine hydroxylase, a specific marker for dopaminergic neurons, immunohistochemical staining. Dissociated cell cultures are prepared from embryonic rats. The culture medium is changed every third day and the factors are also added at that time.

[1205] Since the dopaminergic neurons are isolated from animals at gestation day 14, a developmental time which is past the stage when the dopaminergic precursor cells are proliferating, an increase in the number of tyrosine hydroxylase immunopositive neurons would represent an increase in the number of dopaminergic neurons surviving *in vitro*. Therefore, if a therapeutic protein of the invention acts to prolong the survival of dopaminergic neurons, it would suggest that the fusion protein may be involved in Parkinson's Disease.

EXAMPLE 64: Pancreatic Beta-Cell Transplantation Combination Therapy.

[1206] Transplantation is a common form of treatment of autoimmune disease, especially when the target self tissue has been severely damaged. For example, and not by way of limitation, pancreas transplantation and islet cell transplantation are common treatment options for IDDM (See, e.g., Stewart et al., *Journal of Clinical Endocrinology & Metabolism* 86 (3): 984-988 (2001); Brunicardi, *Transplant. Proc.* 28: 2138-40 (1996); Kendall & Robertson, *Diabetes Metab.* 22: 157-163 (1996); Hamano et al., *Kobe J. Med. Sci.* 42: 93-104 (1996); Larsen & Stratta, *Diabetes Metab.* 22: 139-146 (1996); and Kinkhabwala, et al., *Am. J. Surg.* 171: 516-520 (1996)). As with any transplantation method, transplantation therapies for autoimmune disease patients include treatments to minimize the risk of host rejection of the transplanted tissue. However, autoimmune disease involves the additional, independent risk that the pre-existing host autoimmune response which damaged the original self tissue will exert the same damaging effect on the transplanted tissue. Accordingly, the present invention encompasses methods and compositions for the treatment of autoimmune pancreatic disease using the albumin fusion proteins of the subject invention in combination with immunomodulators/immunosuppressants in individuals undergoing transplantation therapy of the autoimmune disease.

[1207] In accordance with the invention, the albumin fusion-based compositions and formulations described above, are administered to prevent and treat damage to the transplanted organ, tissue, or cells resulting from the host individual's autoimmune response initially directed against the original self tissue. Administration may be carried out both prior and subsequent to transplantation in 2 to 4 doses each one week apart.

[1208] The following immunomodulators/immunosuppressants including, but not limited to, AI-401, CDP-571 (anti-TNF monoclonal antibody), CG-1088, Diamyd (diabetes vaccine), ICM3 (anti-ICAM-3 monoclonal antibody), linomide (Roquinimex), NBI-6024 (altered peptide ligand), TM-27, VX-740 (HMR-3480), caspase 8 protease inhibitors, thalidomide, hOKT3gamma1 (Ala-ala) (anti-CD3 monoclonal antibody), Oral Interferon-Alpha, oral lactobacillus, and LymphoStat-B™ can be used together with the albumin fusion therapeutics of the subject invention in islet cell or pancreas transplantation.

EXAMPLE 65: Identification and Cloning of VH and VL domains.

[1209] One method to identify and clone VH and VL domains from cell lines expressing a particular antibody is to perform PCR with VH and VL specific primers on cDNA made from the antibody expressing cell lines. Briefly, RNA is isolated from the cell lines and used as a template for RT-PCR designed to amplify the VH and VL domains of the antibodies expressed by the EBV cell lines. Cells may be lysed in the TRIzol® reagent (Life Technologies, Rockville, MD) and extracted with one fifth volume of chloroform. After addition of chloroform, the solution is allowed to incubate at room temperature for 10 minutes, and the centrifuged at 14,000 rpm for 15 minutes at 4°C in a tabletop centrifuge. The supernatant is collected and RNA is precipitated using an equal volume of isopropanol. Precipitated RNA is pelleted by centrifuging at 14,000 rpm for 15 minutes at 4°C in a tabletop centrifuge. Following centrifugation, the supernatant is discarded and washed with 75% ethanol. Following washing, the RNA is centrifuged again at 800 rpm for 5 minutes at 4°C. The supernatant is discarded and the pellet allowed to air dry. RNA is dissolved in DEPC water and heated to 60°C for 10 minutes. Quantities of RNA can be determined using optical density measurements.

cDNA may be synthesized, according to methods well-known in the art, from 1.5-2.5 micrograms of RNA using reverse transcriptase and random hexamer primers. cDNA is then

used as a template for PCR amplification of VH and VL domains. Primers used to amplify VH and VL genes are shown in Table 7. Typically a PCR reaction makes use of a single 5' primer and a single 3' primer. Sometimes, when the amount of available RNA template is limiting, or for greater efficiency, groups of 5' and/or 3' primers may be used. For example, sometimes all five VH-5' primers and all JH3' primers are used in a single PCR reaction. The PCR reaction is carried out in a 50 microliter volume containing 1X PCR buffer, 2mM of each dNTP, 0.7 units of High Fidelity Taq polymerase, 5' primer mix, 3' primer mix and 7.5 microliters of cDNA. The 5' and 3' primer mix of both VH and VL can be made by pooling together 22 pmole and 28 pmole, respectively, of each of the individual primers. PCR conditions are: 96°C for 5 minutes; followed by 25 cycles of 94°C for 1 minute, 50°C for 1 minute, and 72°C for 1 minute; followed by an extension cycle of 72°C for 10 minutes. After the reaction is completed, sample tubes are stored 4°C.

Table 7: Primer Sequences Used to Amplify VH and VL domains.

<u>Primer name</u>	<u>SEQ ID NO</u>	<u>Primer Sequence (5'-3')</u>
VH Primers		
Hu VH1-5'	62	CAGGTGCAGCTGGTGCAGTCTGG
Hu VH2-5'	63	CAGGTCAACTTAAGGGAGTCTGG
Hu VH3-5'	64	GAGGTGCAGCTGGTGGAGTCTGG
Hu VH4-5'	65	CAGGTGCAGCTGCAGGAGTCGGG
Hu VH5-5'	66	GAGGTGCAGCTGTTGCAGTCTGC
Hu VH6-5'	67	CAGGTACAGCTGCAGCAGTCAGG
Hu JH1,2-5'	68	TGAGGAGACGGTGACCAGGGTGCC
Hu JH3-5'	69	TGAAGAGACGGTGACCATTTGTCCC
Hu JH4,5-5'	70	TGAGGAGACGGTGACCAGGGTCC
Hu JH6-5'	71	TGAGGAGACGGTGACCGTGGTCCC
VL Primers		
Hu Vkappa1-5'	72	GACATCCAGATGACCCAGTCTCC
Hu Vkappa2a-5'	73	GATGTTGTGATGACTCAGTCTCC
Hu Vkappa2b-5'	74	GATATTGTGATGACTCAGTCTCC
Hu Vkappa3-5'	75	GAAATTGTGTTGACGCAGTCTCC
Hu Vkappa4-5'	76	GACATCGTGATGACCCAGTCTCC
Hu Vkappa5-5'	77	GAAACGACACTCACGCAGTCTCC
Hu Vkappa6-5'	78	GAAATTGTGCTGACTCAGTCTCC
Hu Vlambda1-5'	79	CAGTCTGTGTTGACGCAGCCGCC
Hu Vlambda2-5'	80	CAGTCTGCCCTGACTCAGCCTGC
Hu Vlambda3-5'	81	TCCTATGTGCTGACTCAGCCACC
Hu Vlambda3b-5'	82	TCTTCTGAGCTGACTCAGGACCC
Hu Vlambda4-5'	83	CACGTTATACTGACTCAACCGCC
Hu Vlambda5-5'	84	CAGGCTGTGCTCACTCAGCCGTC
Hu Vlambda6-5'	85	AATTTTATGCTGACTCAGCCCCA
Hu Jkappa1-3'	86	ACGTTTGATTTCCACCTTGGTCCC
Hu Jkappa2-3'	87	ACGTTTGATCTCCAGCTTGGTCCC
Hu Jkappa3-3'	88	ACGTTTGATATCCACTTTGGTCCC
Hu Jkappa4-3'	89	ACGTTTGATCTCCACCTTGGTCCC
Hu Jkappa5-3'	90	ACGTTTAATCTCCAGTCGTGTCCC
Hu Jlambda1-3'	91	CAGTCTGTGTTGACGCAGCCGCC
Hu Jlambda2-3'	92	CAGTCTGCCCTGACTCAGCCTGC
Hu Jlambda3-3'	93	TCCTATGTGCTGACTCAGCCACC
Hu Jlambda3b-3'	94	TCTTCTGAGCTGACTCAGGACCC
Hu Jlambda4-3'	95	CACGTTATACTGACTCAACCGCC
Hu Jlambda5-3'	96	CAGGCTGTGCTCACTCAGCCGTC
Hu Jlambda6-3'	97	AATTTTATGCTGACTCAGCCCCA

PCR samples are then electrophoresed on a 1.3% agarose gel. DNA bands of the expected sizes (~506 base pairs for VH domains, and 344 base pairs for VL domains) can be cut out of the gel and purified using methods well known in the art. Purified PCR products can be ligated into a PCR cloning vector (TA vector from Invitrogen Inc., Carlsbad, CA). Individual cloned PCR products can be isolated after transfection of *E. coli* and blue/white color selection. Cloned PCR products may then be sequenced using methods commonly known in the art.

[1210] The PCR bands containing the VH domain and the VL domains can also be used to create full-length Ig expression vectors. VH and VL domains can be cloned into vectors containing the nucleotide sequences of a heavy (e.g., human IgG1 or human IgG4) or light chain (human kappa or human lambda) constant regions such that a complete heavy or light chain molecule could be expressed from these vectors when transfected into an appropriate host cell. Further, when cloned heavy and light chains are both expressed in one cell line (from either one or two vectors), they can assemble into a complete functional antibody molecule that is secreted into the cell culture medium. Methods using polynucleotides encoding VH and VL antibody domain to generate expression vectors that encode complete antibody molecules are well known within the art.

EXAMPLE 66: Preparation of HA-cytokine or HA-growth factor fusion proteins (such as NGF, BDNFa, BDNFb and BDNFc).

[1211] The cDNA for the cytokine or growth factor of interest, such as NGF, can be isolated by a variety of means including from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The nucleotide sequences for all of these proteins are known and available. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. NGF (or other cytokine) cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines, a similar procedure

is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 67: Preparation of HA-IFN fusion proteins (such as IFN α).

[1212] The cDNA for the interferon of interest such as IFN α can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The nucleotide sequences for interferons, such as IFN α are known and available, for instance, in U.S. Patents 5,326,859 and 4,588,585, in EP 32 134, as well as in public databases such as GenBank. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used to clone the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus of the HA sequence, with or without the use of a spacer sequence. The IFN α (or other interferon) cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

Maximum protein recovery from vials

[1213] The albumin fusion proteins of the invention have a high degree of stability even when they are packaged at low concentrations. In addition, in spite of the low protein concentration, good fusion-protein recovery is observed even when the aqueous solution includes no other protein added to minimize binding to the vial walls. The recovery of vial-stored HA-IFN solutions was compared with a stock solution. 6 or 30 $\mu\text{g/ml}$ HA-IFN solutions were placed in vials and stored at 4°C. After 48 or 72 hrs a volume originally equivalent to 10 ng of sample was removed and measured in an IFN sandwich ELISA. The

estimated values were compared to that of a high concentration stock solution. As shown, there is essentially no loss of the sample in these vials, indicating that addition of exogenous material such as albumin is not necessary to prevent sample loss to the wall of the vials

In vivo stability and bioavailability of HA- α -IFN fusions

[1214] To determine the in vivo stability and bioavailability of a HA- α -IFN fusion molecule, the purified fusion molecule (from yeast) was administered to monkeys. Pharmaceutical compositions formulated from HA- α -IFN fusions may account for the extended serum half-life and bioavailability. Accordingly, pharmaceutical compositions may be formulated to contain lower dosages of alpha-interferon activity compared to the native alpha-interferon molecule.

[1215] Pharmaceutical compositions containing HA- α -IFN fusions may be used to treat or prevent disease in patients with any disease or disease state that can be modulated by the administration of α -IFN. Such diseases include, but are not limited to, hairy cell leukemia, Kaposi's sarcoma, genital and anal warts, chronic hepatitis B, chronic non-A, non-B hepatitis, in particular hepatitis C, hepatitis D, chronic myelogenous leukemia, renal cell carcinoma, bladder carcinoma, ovarian and cervical carcinoma, skin cancers, recurrent respirator papillomatosis, non-Hodgkin's and cutaneous T-cell lymphomas, melanoma, multiple myeloma, AIDS, multiple sclerosis, glioblastoma, etc. (see Interferon Alpha, In: AHFS Drug Information, 1997.

[1216] Accordingly, the invention includes pharmaceutical compositions containing a HA- α -IFN fusion protein, polypeptide or peptide formulated with the proper dosage for human administration. The invention also includes methods of treating patients in need of such treatment comprising at least the step of administering a pharmaceutical composition containing at least one HA- α -IFN fusion protein, polypeptide or peptide.

Bifunctional HA- α -IFN fusions

[1217] A HA- α -IFN expression vector may be modified to include an insertion for the expression of bifunctional HA- α -IFN fusion proteins. For instance, the cDNA for a second protein of interest may be inserted in frame downstream of the "rHA-IFN" sequence after the double stop codon has been removed or shifted downstream of the coding sequence.

[1218] In one version of a bifunctional HA- α -IFN fusion protein, an antibody or

fragment against B-lymphocyte stimulator protein (GenBank Acc 4455139) or polypeptide may be fused to one end of the HA component of the fusion molecule. This bifunctional protein is useful for modulating any immune response generated by the α -IFN component of the fusion.

EXAMPLE 68: Preparation of HA-hormone fusion protein

[1219] The cDNA for the hormone of interest can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The nucleotide sequences for all of these proteins are known and available, for instance, in public databases such as GenBank. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. The hormone cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 69: Preparation of HA-soluble receptor or HA-binding protein fusion protein.

[1220] The cDNA for the soluble receptor or binding protein of interest can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The nucleotide sequences for all of these proteins are known and available, for instance, in GenBank. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or

without the use of a spacer sequence. The receptor cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 70: Preparation of HA-growth factors.

[1221] The cDNA for the growth factor of interest can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods (see GenBank Acc. No.NP_000609). The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. The growth factor cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 71: Preparation of HA-single chain antibody fusion proteins.

[1222] Single chain antibodies are produced by several methods including but not limited to: selection from phage libraries, cloning of the variable region of a specific antibody by cloning the cDNA of the antibody and using the flanking constant regions as the primer to clone the variable region, or by synthesizing an oligonucleotide corresponding to the variable

region of any specific antibody. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. The cell cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast.

[1223] In fusion molecules of the invention, the V_H and V_L can be linked by one of the following means or a combination thereof: a peptide linker between the C-terminus of the V_H and the N-terminus of the V_L ; a Kex2p protease cleavage site between the V_H and V_L such that the two are cleaved apart upon secretion and then self associate; and cystine residues positioned such that the V_H and V_L can form a disulphide bond between them to link them together. An alternative option would be to place the V_H at the N-terminus of HA or an HA domain fragment and the V_L at the C-terminus of the HA or HA domain fragment.

[1224] The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines. The antibody produced in this manner can be purified from media and tested for its binding to its antigen using standard immunochemical methods.

EXAMPLE 72: Preparation of HA-cell adhesion molecule fusion proteins.

[1225] The cDNA for the cell adhesion molecule of interest can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The nucleotide sequences for the known cell adhesion molecules are known and available, for instance, in GenBank. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. The cell adhesion molecule cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete

expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 73: Preparation of inhibitory factors and peptides as HA fusion proteins (such as HA-antiviral, HA-antibiotic, HA-enzyme inhibitor and HA-anti-allergic proteins).

[1226] The cDNA for the peptide of interest such as an antibiotic peptide can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. The peptide cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 74: Preparation of targeted HA fusion proteins.

[1227] The cDNA for the protein of interest can be isolated from cDNA library or can be made synthetically using several overlapping oligonucleotides using standard molecular biology methods. The appropriate nucleotides can be engineered in the cDNA to form convenient restriction sites and also allow the attachment of the protein cDNA to albumin

cDNA. Also a targeting protein or peptide cDNA such as single chain antibody or peptides, such as nuclear localization signals, that can direct proteins inside the cells can be fused to the other end of albumin. The protein of interest and the targeting peptide is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA which allows the fusion with albumin cDNA. In this manner both N- and C-terminal end of albumin are fused to other proteins. The fused cDNA is then excised from pPPC0005 and is inserted into a plasmid such as pSAC35 to allow the expression of the albumin fusion protein in yeast. All the above procedures can be performed using standard methods in molecular biology. The albumin fusion protein secreted from yeast can be collected and purified from the media and tested for its biological activity and its targeting activity using appropriate biochemical and biological tests.

EXAMPLE 75: Preparation of HA-enzymes fusions.

[1228] The cDNA for the enzyme of interest can be isolated by a variety of means including but not exclusively, from cDNA libraries, by RT-PCR and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods. The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for HA. This can be at the N or C-terminus with or without the use of a spacer sequence. The enzyme cDNA is cloned into a vector such as pPPC0005 (Figure 2), pScCHSA, pScNHSA, or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the albumin fusion protein in yeast. The albumin fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator (See Example 1). This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

EXAMPLE 76: Construct ID 2294, BNP-HSA, Generation.

[1229] Construct ID 3448, pC4:BNP/HSA, comprises DNA encoding the HSA leader sequence followed by a BNP-HSA fusion protein which has the processed, active BNP peptide (32 amino acids) fused to the amino-terminus of the mature form of HSA cloned into

the mammalian expression vector pC4.

Cloning of BNP cDNA for construct 3448

[1230] The DNA encoding BNP was amplified with primers BNP1 and BNP2, described below, cut with *Xho* I and *Cla* I, and ligated into *Xho* I/*Cla* I cut pC4:HSA. Construct ID #3448 encodes an albumin fusion protein containing the HSA leader sequence and the processed, active form of BNP, followed by the mature HSA protein (see SEQ ID NO:211 for construct 3448 in Table 2).

[1231] Two oligonucleotides suitable for PCR amplification of the polynucleotide encoding the active, processed form of BNP, BNP1 and BNP2, were synthesized.

BNP1: 5'- CCGCCGCTCGAGGGGTGTGTTTCGTCTGAAGCCCCAAGATGGTGCAAGG
-3' (SEQ ID NO: 105)

BNP2: 5'-

AGTCCCATCGATGAGCAACCTCACTCTTGTGTGCATCATGCCGCCTCAGCACTT
TGC -3' (SEQ ID NO: 106)

BNP1 incorporates a *Bam* HI cloning site (underlined) prior to the last 16 nucleotides of the HSA leader sequence (italicized) and the DNA encoding the first seven amino acid sequence of BNP (bolded). In BNP2, the underlined sequence is a *Cla* I site, and the DNA following it contains the reverse complement of DNA encoding the last 6 amino acids of BNP and the first 10 amino acids of the mature HSA protein. In BNP2, the bolded sequence is the reverse complement of the last 20 nucleotides of BNP. Using these two primers the BNP protein was PCR amplified. Annealing and extension temperatures and times must be empirically determined for each specific primer pair and template.

[1232] The PCR product was purified (for example, using Wizard PCR Preps DNA Purification System (Promega Corp)) and then digested with *Xho* I and *Cla* I. After further purification of the *Xho* I-*Cla* I fragment by gel electrophoresis, the product was cloned into *Xho* I/*Cla* I digested pC4:HSA to produce construct ID # 3448. The construct was sequence verified.

EXAMPLE 77: Construct ID 2053, IFNb-HSA, Generation.

[1233] Construct ID 2053, pEE12.1:IFNb.HSA, comprises DNA encoding an IFNb albumin fusion protein which has the full-length IFNb protein including the native IFNb

leader sequence fused to the amino-terminus of the mature form of HSA in the NS0 expression vector pEE12.1.

Cloning of IFNb cDNA

[1234] The polynucleotide encoding IFNb was PCR amplified using primers IFNb-1 and IFNb-2, described below, cut with *Bam* HI/*Cla* I, and ligated into *Bam* HI/*Cla* I cut pC4:HSA, resulting in construct 2011. The *Eco* RI/*Eco* RI fragment from Construct ID # 2011 was subcloned into the *Eco* RI site of pEE12.1 generating construct ID #2053 which comprises DNA encoding an albumin fusion protein containing the leader sequence and the mature form of IFNb, followed by the mature HSA protein.

[1235] Two oligonucleotides suitable for PCR amplification of the polynucleotide encoding the full-length of IFNb, IFNb-1 and IFNb-2, were synthesized:

IFNb-1: 5'- GCGCGGATCCGAATTCGCGCCGCGCATGACCAACAAGTGTCTCCTCCA
AATTGCTCTCCTGTTGTGCTTCTCCACTACAGCTCTTTCCATGAGCTACAACCTTGC
TTGG-3' (SEQ ID NO:107)

IFNb-2: 5'- GCGCGCATCGATGAGCAACCTCACTCTTGTGTGCATCGTTTCGGA
GGTAACCTGT-3' (SEQ ID NO:108)

[1236] The IFNb-1 primer incorporates a *Bam* HI cloning site (shown underlined), an *Eco* RI cloning site, and a Kozak sequence (shown in italics), followed by 80 nucleotides encoding the first 27 amino acids of the full-length form of IFNb. In IFNb-2, the *Cla* I site (shown underlined) and the DNA following it are the reverse complement of DNA encoding the first 10 amino acids of the mature HSA protein (SEQ ID NO:1) and the last 18 nucleotides are the reverse complement of DNA encoding the last 6 amino acid residues of IFNb (see Example 2). A PCR amplicon was generated using these primers, purified, digested with *Bam* HI and *Cla* I restriction enzymes, and cloned into the *Bam* HI and *Cla* I sites of the pC4:HSA vector. After the sequence was confirmed, an *Eco* RI fragment containing the IFNb albumin fusion protein expression cassette was subcloned into *Eco* RI digested pEE12.1.

[1237] Further, analysis of the N-terminus of the expressed albumin fusion protein by amino acid sequencing can confirm the presence of the expected IFNb sequence (see below).

[1238] IFNb albumin fusion proteins of the invention preferably comprise the mature form of HSA, i.e., Asp-25 to Leu-609, fused to either the N- or C- terminus of the mature form of IFNb, i.e., Met-22 to Asn-187. In one embodiment of the invention, IFNb albumin

fusion proteins of the invention further comprise a signal sequence which directs the nascent fusion polypeptide in the secretory pathways of the host used for expression. In a further preferred embodiment, the signal peptide encoded by the signal sequence is removed, and the mature IFNb albumin fusion protein is secreted directly into the culture medium. IFNb albumin fusion proteins of the invention may comprise heterologous signal sequences including, but not limited to, MAF, INV, Ig, Fibulin B, Clusterin, Insulin-Like Growth Factor Binding Protein 4, variant HSA leader sequences including, but not limited to, a chimeric HSA/MAF leader sequence, or other heterologous signal sequences known in the art. In a preferred embodiment, IFNb albumin fusion proteins of the invention comprise the native IFNb. In further preferred embodiments, the IFNb albumin fusion proteins of the invention further comprise an N-terminal methionine residue. Polynucleotides encoding these polypeptides, including fragments and/or variants, are also encompassed by the invention.

Expression and Purification of Construct ID 2053.

Expression in murine myeloma NS0 cell-lines.

[1239] Construct ID # 2053, pEE12.1:IFNb-HSA, was electroporated into NS0 cells by methods known in the art (see Example 6).

Purification from NS0 cell supernatant.

[1240] Purification of IFNb-HSA from NS0 cell supernatant may involve Q-Sepharose anion exchange chromatography at pH 7.4 using a NaCl gradient from 0 to 1 M in 20 mM Tris-HCl, followed by Poros PI 50 anion exchange chromatography at pH 6.5 with a sodium citrate gradient from 5 to 40 mM, and diafiltrating for 6 DV into 10 mM citrate, pH 6.5 and 140 mM NaCl, the final buffer composition. N-terminal sequencing should yield the sequence MSYNLL which is the amino terminus of the mature form of IFNb. The protein has an approximate MW of 88.5 kDa.

[1241] For larger scale purification, e.g., 50 L of NS0 cell supernatant can be concentrated into ~8 to 10 L. The concentrated sample can then be passed over the Q-Sepharose anion exchange column (10 x 19 cm, 1.5 L) at pH 7.5 using a step elution consisting of 50 mM NaOAc, pH 6.0 and 150 mM NaCl. The eluted sample can then be virally inactivated with 0.75% Triton-X 100 for 60 min at room temperature. SDR-Reverse Phase chromatography (10 cm x 10 cm, 0.8 L) can then be employed at pH 6.0 with 50 mM NaOAc and 150 mM NaCl, or alternatively, the sample can be passed over an SP-sepharose

column at pH 4.8 using a step elution of 50 mM NaOAc, pH 6.0, and 150 mM NaCl. DV 50 filtration would follow to remove any viral content. Phenyl-650M chromatography (20 cm x 12 cm, 3.8 L) at pH 6.0 using a step elution consisting of 350 mM $(\text{NH}_4)_2\text{SO}_4$ and 50 mM NaOAc, or alternatively consisting of 50 mM NaOAc pH 6.0, can follow. Diafiltration for 6-8 DV will allow for buffer exchange into the desired final formulation buffer of either 10 mM Na_2HPO_4 + 58 mM sucrose + 120 mM NaCl, pH 7.2 or 10 mM citrate, pH 6.5, and 140 mM NaCl or 25 mM Na_2HPO_4 , 100 mM NaCl, pH 7.2.

The activity of IFNb can be assayed using an in vitro ISRE-SEAP assay.

[1242] All type I Interferon proteins signal through a common receptor complex and a similar Jak/STAT signaling pathway that culminates in the activation of Interferon, "IFN", responsive genes through the Interferon Sequence Responsive Element, "ISRE". A convenient assay for type I IFN activity is a promoter-reporter based assay system that contains multiple copies of the ISRE element fused to a downstream reporter gene. A stable HEK293 cell-line can be generated and contains a stably integrated copy of an ISRE-SEAP reporter gene that is extremely sensitive to type I IFNs and displays linearity over 5 logs of concentration.

Method of Screening of IFNb-HSA NS0 stable clones.

[1243] Construct 2053 was electroporated into NS0 cells as described in Example 6. The NS0 cells transfected with construct ID # 2053 were screened for activity by testing conditioned growth media in the ISRE-SEAP assay. The ISRE-SEAP/293F reporter cells were plated at 3×10^4 cell/well in 96-well, poly-D-lysine coated, plates, one day prior to treatment. Reporter cells were treated with various dilutions (including but not limited to 1:500 and 1:5000) of conditioned supernatant or purified preparations of IFNb albumin fusion protein encoded by construct ID 2053 or rhIFNb as a control. The reporter cells were then incubated for 24 hours prior to removing 40 μL for use in the SEAP Reporter Gene Chemiluminescent Assay (Roche catalog # 1779842). Recombinant human Interferon beta, "rhIFNb" (Biogen), was used as a positive control.

Result

[1244] The purified preparation of NS0 expressed IFNb-HSA had a greater EC_{50} of 9.3×10^{-9} g/mL than rhIFNb (Biogen) which had an EC_{50} of 1.8×10^{-10} g/mL (see Figure 5).

*In vivo induction of OAS by an Interferon.**Method*

[1245] The OAS enzyme, 2'-5'- OligoAdenylate Synthetase, is activated at the transcriptional level by interferon in response to antiviral infection. The effect of interferon constructs can be measured by obtaining blood samples from treated monkeys and analyzing these samples for transcriptional activation of two OAS mRNA, p41 and p69. A volume of 0.5 mL of whole blood can be obtained from 4 animals per group at 7 different time points, day 0, day 1, day 2, day 4, day 8, day 10, and day 14 per animal. The various groups may include injection of vehicle control, intravenous and/or subcutaneous injection of either 30 μ g/kg and/or 300 μ g/kg IFN albumin fusion protein on day 1, and subcutaneous injection of 40 μ g/kg of Interferon alpha (Schering-Plough) as a positive control on days 1, 3, and 5. The levels of the p41 and the p69 mRNA transcripts can be determined by real-time quantitative PCR (Taqman) using probes specific for p41-OAS and p69-OAS. OAS mRNA levels can be quantitated relative to 18S ribosomal RNA endogenous control.

*In vivo induction of OAS by Interferon beta albumin fusion encoded by construct ID 2053.**Method*

[1246] The activity of the HSA-IFNb fusion protein encoded by construct 2053 can be assayed in the *in vivo* OAS assay as previously described above under subsection heading, "*In vivo* induction of OAS by an Interferon".

EXAMPLE 78: Indications for IFNb albumin fusion proteins.

[1247] IFN beta albumin fusion proteins (including, but not limited to, those encoded by construct 2053) can be used to treat, prevent, ameliorate and/or detect multiple sclerosis. Other indications include, but are not limited to Viral infections including Severe Acute Respiratory Syndrome (SARS) and other coronavirus infections; filoviruses, including but not limited to Ebola viruses and Marburg virus; Arenaviruses, including but not limited to Pichende virus, Lassa virus, Junin virus, Machupo virus, Guanarito virus; and lymphocytic choriomeningitis virus (LCMV); Bunyaviruses, including but not limited to Punta toro virus, Crimean-Congo hemorrhagic fever virus, sandfly fever viruses, Rift Valley fever virus, La Crosse virus, and hantaviruses; Flaviviruses, including but not limited to Yellow Fever, Banzai virus, West Nile virus, Dengue viruses, Japanese Encephalitis virus, Tick-borne encephalitis,

Omsk Hemorrhagic Fever, and Kyasanur Forest Disease virus; Togaviruses, including but not limited to Venezuelan, eastern, and western equine encephalitis viruses, Ross River virus, and Rubella virus; Orthopox viruses, including but not limited to Vaccinia, Cowpox, Smallpox, and Monkeypox; Herpesviruses; FluA/B; Respiratory Sincytial virus (RSV); parafllu; measles; rhinoviruses; adenoviruses; Semliki Forest virus; Viral Hemorrhagic fevers; Rhabdoviruses; Paramyxoviruses, including but not limited to Nipah virus and Hendra virus; and other viral agents identified by the U.S. Centers for Disease Control and Prevention as high-priority disease agents (*i.e.*, Category A, B, and C agents; see, *e.g.*, Moran, *Emerg. Med. Clin. North. Am.* 2002; 20(2):311-30 and Darling et al., *Emerg. Med. Clin. North Am.* 2002;20(2):273-309).

EXAMPLE 79: Construct ID 2249, IFNa2-HSA, Generation.

[1248] Construct ID 2249, pSAC35:IFNa2.HSA, comprises DNA encoding an IFNa2 albumin fusion protein which has the HSA chimeric leader sequence, followed by the mature form of IFNa2 protein, *i.e.*, C1-E165, fused to the amino-terminus of the mature form of HSA in the yeast *S. cerevisiae* expression vector pSAC35.

Cloning of IFNa2 cDNA

[1249] The polynucleotide encoding IFNa2 was PCR amplified using primers IFNa2-1 and IFNa2-2, described below. The PCR amplimer was cut with *Sal* I/*Cla* I, and ligated into *Xho* I/*Cla* I cut pScHSA. Construct ID #2249 encodes an albumin fusion protein containing the chimeric leader sequence of HSA, the mature form of IFNa2, followed by the mature HSA protein.

[1250] Two oligonucleotides suitable for PCR amplification of the polynucleotide encoding the mature form of IFNa2, IFNa2-1 and IFNa2-2, were synthesized:

IFNa2-1: 5'-CGCGCGCGTCGACAAAAGATGTGATCTGCCTCAAACCCACA-3' (SEQ ID NO:109)

IFNa2-2: 5'-GCGCGCATCGATGAGCAACCTCACTCTTGTGTGCATCTTCCTTAC TTCTTAAACTTTCT-3' (SEQ ID NO:110)

[1251] The IFNa2-1 primer incorporates a *Sal* I cloning site (shown underlined), nucleotides encoding the last three amino acid residues of the chimeric HSA leader sequence,

as well as 22 nucleotides (shown in bold) encoding the first 7 amino acid residues of the mature form of IFNa2. In IFNa2-2, the *Cla* I site (shown underlined) and the DNA following it are the reverse complement of DNA encoding the first 10 amino acids of the mature HSA protein and the last 22 nucleotides (shown in bold) are the reverse complement of DNA encoding the last 7 amino acid residues of IFNa2 (see Example 2). A PCR amplicon of IFNa2-HSA was generated using these primers, purified, digested with *Sal* I and *Cla* I restriction enzymes, and cloned into the *Xho* I and *Cla* I sites of the pScCHSA vector. After the sequence was confirmed, the expression cassette encoding this IFNa2 albumin fusion protein was subcloned into *Not* I digested pSAC35.

[1252] Further, analysis of the N-terminus of the expressed albumin fusion protein by amino acid sequencing can confirm the presence of the expected IFNa2 sequence (see below).

[1253] Other IFNa2 albumin fusion proteins using different leader sequences have been constructed by methods known in the art (see Example 2). Examples of the various leader sequences include, but are not limited to, invertase "INV" (constructs 2343 and 2410) and mating alpha factor "MAF" (construct 2366). These IFNa2 albumin fusion proteins can be subcloned into mammalian expression vectors such as pC4 (constructs 2382) and pEE12.1 as described previously (see Example 5). IFNa2 albumin fusion proteins with the therapeutic portion fused C-terminus to HSA can also be constructed (construct 2381).

[1254] IFNa2 albumin fusion proteins of the invention preferably comprise the mature form of HSA, i.e., Asp-25 to Leu-609, fused to either the N- or C- terminus of the mature form of IFNa2, i.e., Cys-1 to Glu-165. In one embodiment of the invention, IFNa2 albumin fusion proteins of the invention further comprise a signal sequence which directs the nascent fusion polypeptide in the secretory pathways of the host used for expression. In a further preferred embodiment, the signal peptide encoded by the signal sequence is removed, and the mature IFNa2 albumin fusion protein is secreted directly into the culture medium. IFNa2 albumin fusion proteins of the invention may comprise heterologous signal sequences including, but not limited to, MAF, INV, Ig, Fibulin B, Clusterin, Insulin-Like Growth Factor Binding Protein 4, variant HSA leader sequences including, but not limited to, a chimeric HSA/MAF leader sequence, or other heterologous signal sequences known in the art. In a preferred embodiment, IFNa2 albumin fusion proteins of the invention comprise the native IFNa2. In further preferred embodiments, the IFNa2 albumin fusion proteins of the invention further comprise an N-terminal methionine residue. Polynucleotides encoding these

polypeptides, including fragments and/or variants, are also encompassed by the invention.

Expression and Purification of Construct ID 2249.

Expression in yeast S. cerevisiae.

[1255] Transformation of construct 2249 into yeast *S. cerevisiae* strain BXP10 was carried out by methods known in the art (see Example 3). Cells can be collected at stationary phase after 72 hours of growth. Supernatants are collected by clarifying cells at 3000g for 10 min. Expression levels are examined by immunoblot detection with anti-HSA serum (Kent Laboratories) or as the primary antibody. The IFNa2 albumin fusion protein of approximate molecular weight of 88.5 kDa can be obtained.

Purification from yeast S. cerevisiae cell supernatant.

[1256] The cell supernatant containing IFNa2 albumin fusion protein expressed from construct ID #2249 in yeast *S. cerevisiae* cells can be purified either small scale over a Dyax peptide affinity column (see Example 4) or large scale by following 5 steps: diafiltration, anion exchange chromatography using DEAE-Sepharose Fast Flow column, hydrophobic interaction chromatography (HIC) using Butyl 650S column, cation exchange chromatography using an SP-Sepharose Fast Flow column or a Blue-Sepharose chromatography, and high performance chromatography using Q-sepharose high performance column chromatography (see Example 4). The IFNa2 albumin fusion protein may elute from the DEAE-Sepharose Fast Flow column with 100 – 250 mM NaCl, from the SP-Sepharose Fast Flow column with 150 – 250 mM NaCl, and from the Q-Sepharose High Performance column at 5 – 7.5 mS/cm. N-terminal sequencing should yield the sequence CDLPQ (SEQ ID NO:98) which corresponds to the mature form of IFNa2.

The activity of IFNa2 can be assayed using an in vitro ISRE-SEAP assay.

Method

[1257] The IFNa2 albumin fusion protein encoded by construct ID # 2249 can be tested for activity in the ISRE-SEAP assay as previously described in Example 77. Briefly, conditioned yeast supernatants were tested at a 1:1000 dilution for their ability to direct ISRE signal transduction on the ISRE-SEAP/293F reporter cell-line. The ISRE-SEAP/293F reporter cells were plated at 3×10^4 cell/well in 96-well, poly-D-lysine coated, plates, one day prior to treatment. The reporter cells were then incubated for 18 or 24 hours prior to

removing 40 μ L for use in the SEAP Reporter Gene Chemiluminescent Assay (Roche catalog # 1779842). Recombinant human Interferon beta, "rhIFNb" (Biogen), was used as a positive control.

Result

[1258] The purified preparation of IFNa2-HSA demonstrated a relatively linear increase in the ISRE-SEAP assay over concentrations ranging from 10^{-1} to 10^1 ng/mL (see Figure 6) or 10^{-10} to 10^{-8} ng/mL (see Figure 7).

In vivo induction of OAS by Interferon alpha fusion encoded by construct ID 2249.

Method

[1259] The OAS enzyme, 2'-5'- OligoAdenylate Synthetase, is activated at the transcriptional level by interferon in response to antiviral infection. The effect of interferon constructs can be measured by obtaining blood samples from treated monkeys and analyzing these samples for transcriptional activation of two OAS mRNA, p41 and p69. A volume of 0.5 mL of whole blood was obtained from 4 animals per group at 7 different time points, day 0, day 1, day 2, day 4, day 8, day 10, and day 14 per animal. The various groups include vehicle control, intravenous injection of 30 μ g/kg HSA-IFN on day 1, subcutaneous injection of 30 μ g/kg of HSA-IFN on day 1, subcutaneous injection of 300 μ g/kg of HSA-IFN on day 1, and subcutaneous injection of 40 μ g/kg of Interferon alpha (Schering-Plough) as a positive control on days 1, 3, and 5. The levels of the p41 and the p69 mRNA transcripts were determined by real-time quantitative PCR (Taqman) using probes specific for p41-OAS and p69-OAS. OAS mRNA levels were quantitated relative to 18S ribosomal RNA endogenous control. The albumin fusion encoded by construct 2249 can be subjected to similar experimentation.

Results

[1260] A significant increase in mRNA transcript levels for both p41 and p69 OAS was observed in HSA-interferon treated monkeys in contrast to IFNa treated monkeys (see Figure 8 for p41 data). The effect lasted nearly 10 days.

EXAMPLE 80: Indications for IFNa2 Albumin Fusion Proteins

[1261] IFN alpha albumin fusion protein (including, but not limited to, those encoded by constructs 2249, 2343, 2410, 2366, 2382, and 2381) can be used to treat, prevent,

ameliorate, and/or detect multiple sclerosis. Other indications include, but are not limited to viral infections including Severe Acute Respiratory Syndrome (SARS) and other coronavirus infections; filoviruses, including but not limited to Ebola viruses and Marburg virus; Arenaviruses, including but not limited to Pichende virus, Lassa virus, Junin virus, Machupo virus, Guanarito virus; and lymphocytic choriomeningitis virus (LCMV); Bunyaviruses, including but not limited to Punta toro virus, Crimean-Congo hemorrhagic fever virus, sandfly fever viruses, Rift Valley fever virus, La Crosse virus, and hantaviruses; Flaviviruses, including but not limited to Yellow Fever, Banzai virus, West Nile virus, Dengue viruses, Japanese Encephalitis virus, Tick-borne encephalitis, Omsk Hemorrhagic Fever, and Kyasanur Forest Disease virus; Togaviruses, including but not limited to Venezuelan, eastern, and western equine encephalitis viruses, Ross River virus, and Rubella virus; Orthopox viruses, including but not limited to Vaccinia, Cowpox, Smallpox, and Monkeypox; Herpesviruses; FluA/B; Respiratory Sincytial virus (RSV); parainfluenza; measles; rhinoviruses; adenoviruses; Semliki Forest virus; Viral Hemorrhagic fevers; Rhabdoviruses; Paramyxoviruses, including but not limited to Nipah virus and Hendra virus; and other viral agents identified by the U.S. Centers for Disease Control and Prevention as high-priority disease agents (*i.e.*, Category A, B, and C agents; see, *e.g.*, Moran, *Emerg. Med. Clin. North Am.* 2002; 20(2):311-30 and Darling et al., *Emerg. Med. Clin. North Am.* 2002;20(2):273-309).

[1262] Preferably, the IFN α -albumin fusion protein or IFN hybrid fusion protein is administered in combination with a CCR5 antagonist, further in association with at least one of ribavirin, IL-2, IL-12, pentafuside alone or in combination with an anti-HIV drug therapy, *e.g.*, HAART, for preparation of a medicament for the treatment of HIV-1 infections, HCV, or HIV-1 and HCV co-infections in treatment-naïve as well as treatment-experienced adult and pediatric patients.

[1263] The entire disclosure of each document cited (including patents, patent applications, patent publications, journal articles, abstracts, laboratory manuals, books, or other disclosures) as well as information available through Identifiers specific to databases such as GenBank, GeneSeq, or the CAS Registry, referred to in this application are herein incorporated by reference in their entirety.

[1264] Furthermore, the specification and sequence listing of each of the following U.S. applications are herein incorporated by reference in their entirety: U.S. Application No.

60/441,305, filed January 22, 2003; U.S. Application No. 60/453,201, filed March 11, 2003; U.S. Application No. 60/467,222, filed May 2, 2003; U.S. Application No. 60/472,816, filed May 23, 2003; U.S. Application No. 60/476,267, filed June 6, 2003; U.S. Application No. 60/505,172, filed September 24, 2003; and U.S. Application No. 60/506,746, filed September 30, 2003.

INDICATIONS RELATING TO DEPOSITED BIOLOGICAL MATERIAL

(PCT Rule 13bis)

A. The indications made below relate to the deposited biological material referred to in Table 3 and page 137, paragraph 303 of the description.

B. **IDENTIFICATION OF DEPOSIT:**

Further deposits are identified
on an additional sheet: ☐

Name of Depository: American Type Culture Collection
Address of Depository: 10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

	Accession Number	Date of Deposit		Accession Number	Date of Deposit
1	PTA-3764	Oct-04-2001	2	PTA-3941	Dec-19-2001
3	PTA-3763	Oct-04-2001	4	PTA-3940	Dec-19-2001
5	PTA-3942	Dec-19-2001	6	PTA-3939	Dec-19-2001
7	PTA-3943	Dec-19-2001	8	PTA-4670	Sep-16-2002
9	PTA-4671	Sep-16-2002	10	PTA-3278	
11	PTA-3279		12	PTA-3276	
13	PTA-3277		14		

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

What is claimed:

1. An albumin fusion protein comprising a member selected from the group consisting of:
 - (a) a Therapeutic protein:X and albumin comprising the amino acid sequence of SEQ ID NO:1;
 - (b) a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:1, wherein said fragment or variant has albumin activity;
 - (c) a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:1, wherein said fragment or variant has albumin activity, and further wherein said albumin activity is the ability to prolong the shelf life of the Therapeutic protein:X compared to the shelf-life of the Therapeutic protein:X in an unfused state;
 - (d) a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:1, wherein said fragment or variant has albumin activity, and further wherein the fragment or variant comprises the amino acid sequence of amino acids 1-387 of SEQ ID NO:1;
 - (e) a fragment or variant of a Therapeutic protein:X and albumin comprising the amino acid sequence of SEQ ID NO:1, wherein said fragment or variant has a biological activity of the Therapeutic protein:X;
 - (f) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the N-terminus of albumin, or the N-terminus of the fragment or variant of albumin;
 - (g) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment or variant of albumin;
 - (h) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the N-terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment or variant of albumin;
 - (i) a Therapeutic protein:X, or fragment or variant thereof, and albumin,

or fragment or variant thereof, of (a) to (e), which comprises a first Therapeutic protein:X, or fragment or variant thereof, and a second Therapeutic protein:X, or fragment or variant thereof, wherein said first Therapeutic protein:X, or fragment or variant thereof, is different from said second Therapeutic protein:X, or fragment or variant thereof;

(j) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (i), wherein the Therapeutic protein:X, or fragment or variant thereof, is separated from the albumin or the fragment or variant of albumin by a linker; and

(k) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (j), wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

and further wherein R1 is Therapeutic protein:X, or fragment or variant thereof, L is a peptide linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:1 or a fragment or variant of albumin.

2. The albumin fusion protein of claim 1, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

3. The albumin fusion protein of claim 1, wherein the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

4. The albumin fusion protein of claim 1, wherein the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

5. An albumin fusion protein comprising a Therapeutic protein:X, or fragment or variant thereof, inserted into an albumin, or fragment or variant thereof, comprising the amino

acid sequence of SEQ ID NO:1 or fragment or variant thereof.

6. An albumin fusion protein comprising a Therapeutic protein:X, or fragment or variant thereof, inserted into an albumin, or fragment or variant thereof, comprising an amino acid sequence selected from the group consisting of:

- (a) amino acids 54 to 61 of SEQ ID NO:1;
- (b) amino acids 76 to 89 of SEQ ID NO:1;
- (c) amino acids 92 to 100 of SEQ ID NO:1;
- (d) amino acids 170 to 176 of SEQ ID NO:1;
- (e) amino acids 247 to 252 of SEQ ID NO:1;
- (f) amino acids 266 to 277 of SEQ ID NO:1;
- (g) amino acids 280 to 288 of SEQ ID NO:1;
- (h) amino acids 362 to 368 of SEQ ID NO:1;
- (i) amino acids 439 to 447 of SEQ ID NO:1;
- (j) amino acids 462 to 475 of SEQ ID NO:1;
- (k) amino acids 478 to 486 of SEQ ID NO:1; and
- (l) amino acids 560 to 566 of SEQ ID NO:1.

7. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, as compared to the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

8. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, as compared to the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

9. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin as compared to the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an

unfused state.

10. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin as compared to the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

11. The albumin fusion protein of claim 5 wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin compared to the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

12. The albumin fusion protein of claim 6 wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin compared to the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

13. The albumin fusion protein of any one of claims 1-12, which is non-glycosylated.

14. The albumin fusion protein of any one of claims 1-12, which is expressed in yeast.

15. The albumin fusion protein of claim 14, wherein the yeast is glycosylation deficient.

16. The albumin fusion protein of claim 14 wherein the yeast is glycosylation and protease deficient.

17. The albumin fusion protein of any one of claims 1-12, which is expressed by a mammalian cell.

18. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

19. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein further comprises a secretion leader sequence.

20. A composition comprising the albumin fusion protein of any one of claims 1-12 and a pharmaceutically acceptable carrier.

21. A kit comprising the composition of claim 20.

22. A method of treating a disease or disorder in a patient, comprising the step of administering the albumin fusion protein of any one of claims 1-12.

23. The method of claim 22, wherein the disease or disorder comprises indication:Y.

24. A method of treating a patient with a disease or disorder that is modulated by Therapeutic protein:X, or fragment or variant thereof, comprising the step of administering an effective amount of the albumin fusion protein of any one of claims 1-12.

25. The method of claim 24, wherein the disease or disorder is indication:Y.

26. A method of extending the shelf life of Therapeutic protein:X, or fragment or variant thereof, comprising the step of fusing the Therapeutic protein:X, or fragment or variant thereof, to albumin, or fragment or variant thereof, sufficient to extend the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, compared to the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

27. A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-12.

28. A vector comprising the nucleic acid molecule of claim 27.

29. A host cell comprising the nucleic acid molecule of claim 28.

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Figure 1A

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Figure 1B

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Figure 1C

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Figure 1D

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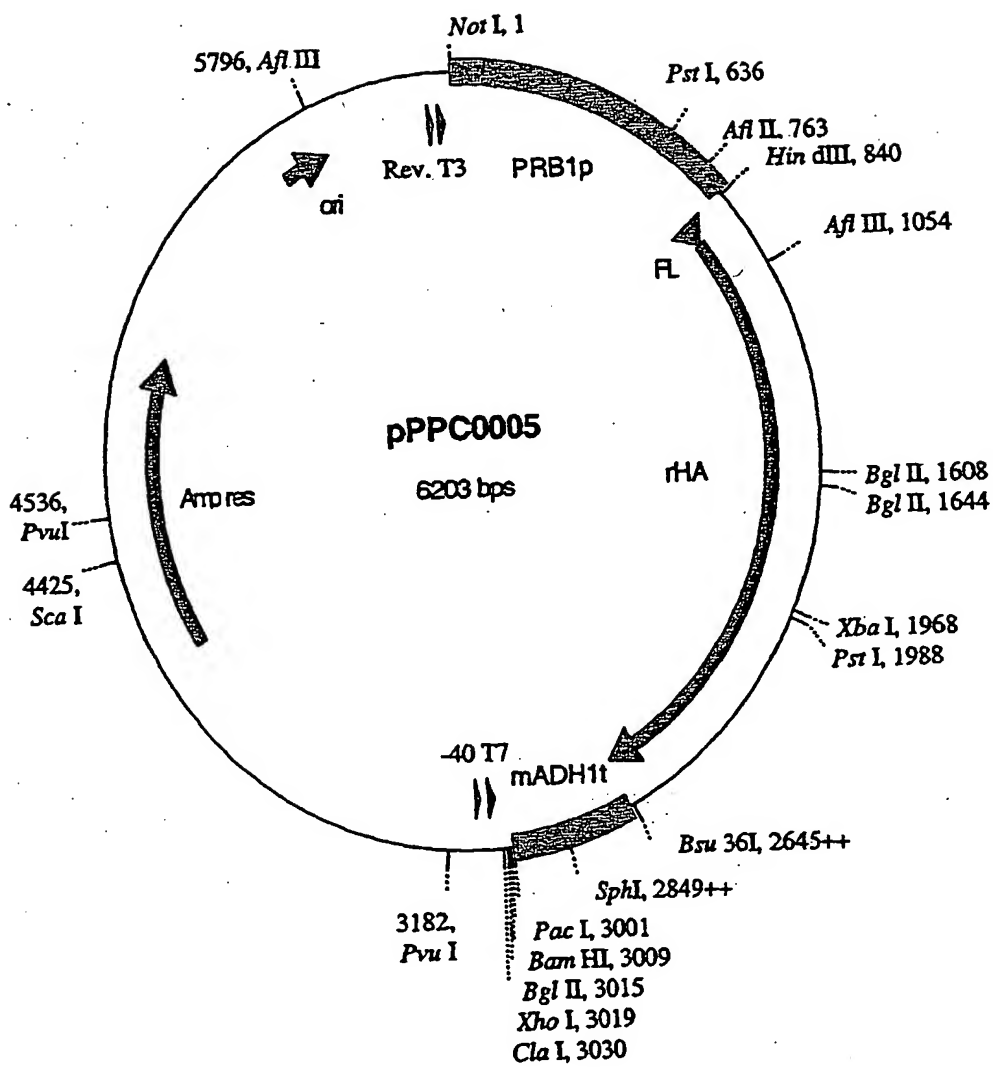


Figure 2

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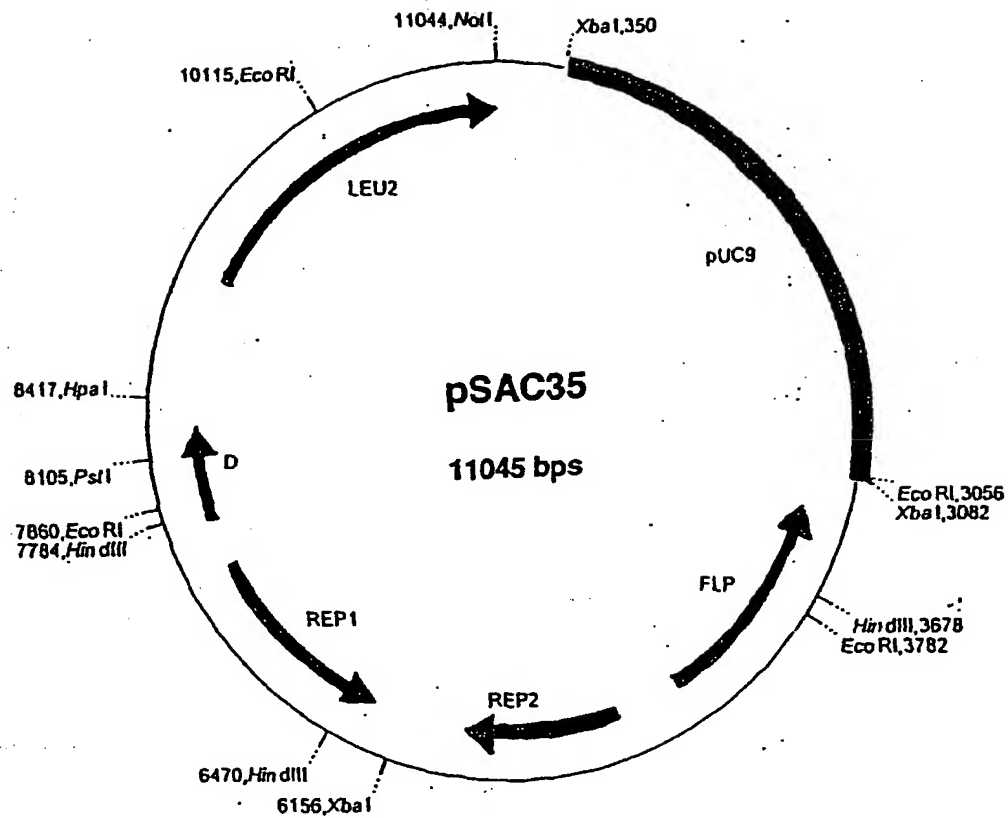
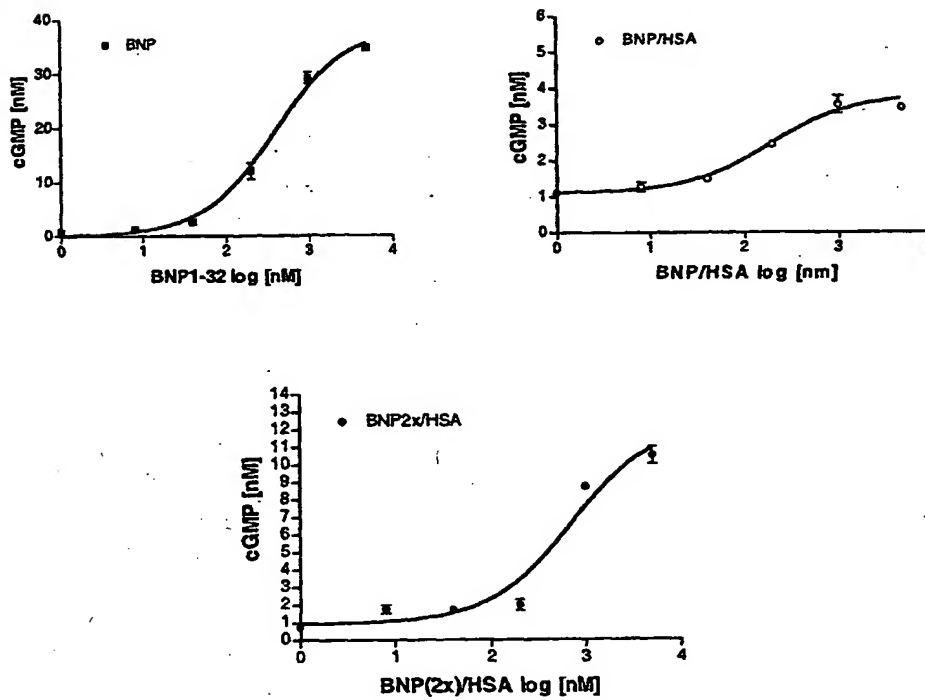


Figure 3

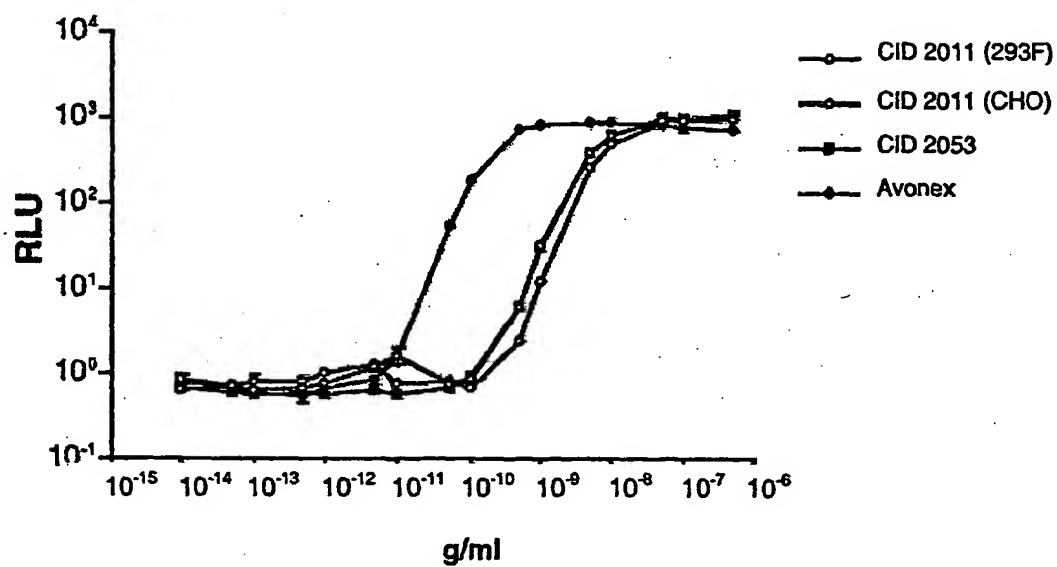
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Lung Fibroblast cGMP Induction ELISA Assay

	BNP	BNP/HSA	BNP2x/HSA
TOP	38.3	3.81	12.3
LOGEC50	2.60	2.28	2.85
EC50	394	189	712

Figure 4

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**Dose response of IFN β albumin
fusion proteins****Figure 5**

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Inhibition of proliferation of HS294T melanoma cells
by IFN α albumin fusion protein

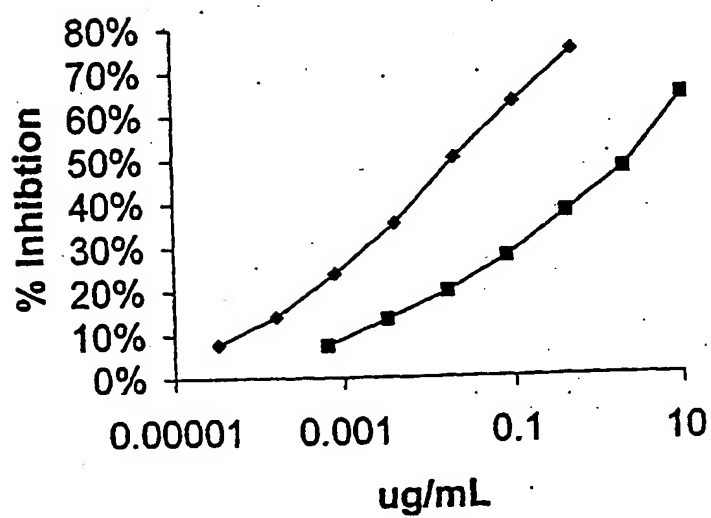
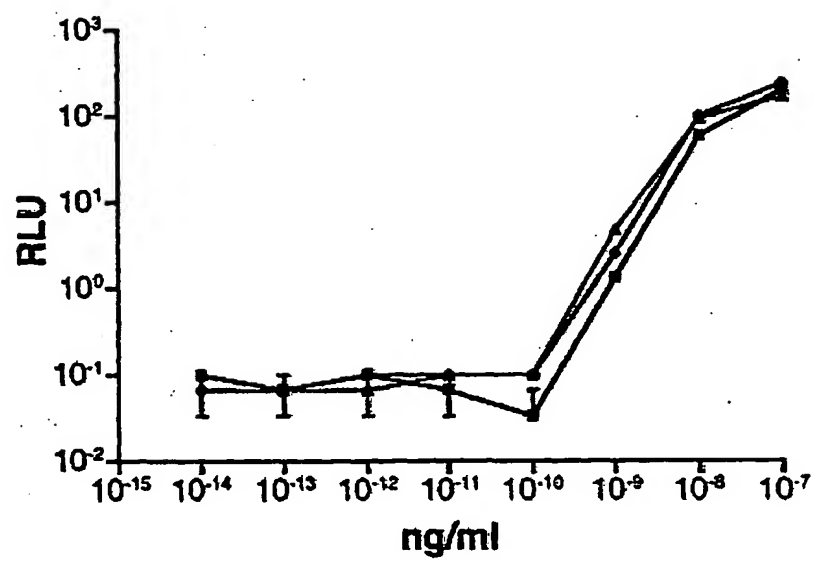


Figure 6

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**SEAP activation with IFN α albumin
fusion proteins****Figure 7**

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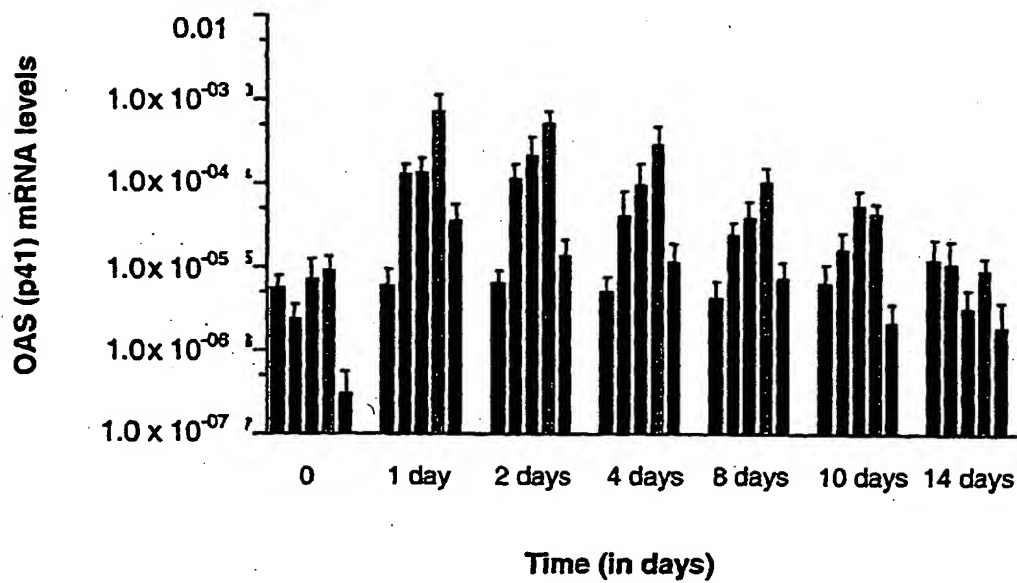


Figure 8

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aaagagcaac tgaaagtgt tatggatgat ttcgcagctt ttgtagagaa gtgctgcaag 1680
gctgacgata agggacctg ctttgccgag gagggtaaaa aacttggtgc tgcaagtcaa 1740
gctgccttag gctta 1755

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<210> 3

<211> 609

<212> PRT

<213> Homo sapiens

<400> 3

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Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
  1                      5                      10                      15

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Tyr Ser Arg Gly Val Phe Arg Arg Asp Ala His Lys Ser Glu Val Ala
      20                      25                      30

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```

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
      35                      40                      45

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```

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
      50                      55                      60

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```

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
      65                      70                      75                      80

```

```

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
      85                      90                      95

```

```

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
      100                      105                      110

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Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
      115                      120                      125

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His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
      130                      135                      140

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```

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
      145                      150                      155                      160

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```

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
      165                      170                      175

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Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480

Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605

Leu

<210> 4
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <221> turn
 <223> Linker peptide that may be used to join VH
 and VL domains in an scFv.

<400> 4
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 5
 <211> 394
 <212> DNA
 <213> Homo sapiens

<400> 5
 gcgccgcgcg gatgcaaggg ttcgaatccc ttagctctca ttattttttg ctttttctct 60
 tgaggtcaca tgatcgcaaa atggcaaatg gcacgtgaag ctgtcgatat tggggaactg 120
 tgggtggttg caaatgacta attaatgtag tcaaggcgcc atcctcatga aaactgtgta 180
 acataataac cgaagtgtcg aaaaggtggc accttgtcca attgaacacg ctcgatgaaa 240
 aaaataagat atatataagg ttaagtaaag cgtctgttag aaaggaagt tttccttttt 300
 cttgtctctt tgtcttttca tctactatct ccttcgtgta atacagggtc gtcagatata 360
 tagatacaat tctattaccc ccatccatac aatg 394

<210> 6
<211> 21
<212> PRT
<213> Homo sapiens

<400> 6
Met Lys Val Ser Val Ala Ala Leu Ser Cys Leu Met Leu Val Thr Ala
1 5 10 15
Leu Gly Ser Gln Ala
20

<210> 7
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> signal
<223> Stanniocalcin signal peptide

<400> 7
Met Leu Gln Asn Ser Ala Val Leu Leu Leu Val Ile Ser Ala Ser
1 5 10 15
Ala

<210> 8
<211> 24
<212> PRT
<213> Homo sapiens

<400> 8
Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15
Tyr Ser Arg Gly Val Phe Arg Arg
20

<210> 9
<211> 18
<212> PRT
<213> Homo sapiens

<400> 9
Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15
Tyr Ser

<210> 10
<211> 18
<212> PRT
<213> Homo sapiens

<400> 10

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser

<210> 11

<211> 19

<212> PRT

<213> Homo sapiens

<400> 11

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15

Ile Ser Ala

<210> 12

<211> 86

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (84)

<223> Xaa equals any one of Glu or Asp

<400> 12

Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Ala Phe Ala Ala Ser
 1 5 10 15

Ser Ala Leu Ala Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala
 20 25 30

Gln Ile Pro Ala Glu Ala Val Ile Gly Tyr Ser Asp Leu Glu Gly Asp
 35 40 45

Phe Asp Val Ala Val Leu Pro Phe Ser Asn Ser Thr Asn Asn Gly Leu
 50 55 60

Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys Glu Glu Gly
 65 70 75 80

Val Ser Leu Xaa Lys Arg
 85

<210> 13

<211> 24

<212> PRT

<213> Homo sapiens

<400> 13

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Glu Lys Arg
20

<210> 14

<211> 24

<212> PRT

<213> Homo sapiens

<400> 14

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg
20

<210> 15

<211> 21

<212> PRT

<213> Homo sapiens

<400> 15

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
1 5 10 15

Ser Leu Asp Lys Arg
20

<210> 16

<211> 19

<212> PRT

<213> Homo sapiens

<400> 16

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser

<210> 17

<211> 29

<212> PRT

<213> Homo sapiens

<400> 17

Met Glu Arg Ala Ala Pro Ser Arg Arg Val Pro Leu Pro Leu Leu Leu
1 5 10 15

Leu Gly Gly Leu Ala Leu Leu Ala Ala Gly Val Asp Ala
20 25

<210> 18

<211> 22

<212> PRT

<213> Homo sapiens

<400> 18

Met Met Lys Thr Leu Leu Leu Phe Val Gly Leu Leu Leu Thr Trp Glu
1 5 10 15

Ser Gly Gln Val Leu Gly
20

<210> 19

<211> 21

<212> PRT

<213> Homo sapiens

<400> 19

Met Leu Pro Leu Cys Leu Val Ala Ala Leu Leu Leu Ala Ala Gly Pro
1 5 10 15

Gly Pro Ser Leu Gly
20

<210> 20

<211> 24

<212> PRT

<213> Homo sapiens

<400> 20

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Gly Val Phe Arg Arg
20

<210> 21

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (18).

<223> Variant of HSA native leader

<400> 21

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ala Gly Val
1 5 10 15

Leu Gly

<210> 22

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (18)

<223> Variant of HSA native leader

<400> 22

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Gly Val
 1 5 10 15

Leu Gly

<210> 23

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (18)

<223> Variant of HSA native leader

<400> 23

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Gly Gly Val
 1 5 10 15

Leu Gly

<210> 24

<211> 18

<212> PRT

<213> Homo sapiens

<400> 24

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ala Gly Val
 1 5 10 15

Ser Gly

<210> 25

<211> 18

<212> PRT

<213> Homo sapiens

<400> 25

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Gly Gly Val
 1 5 10 15

Ser Gly

<210> 26

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (18)

<223> Variant of HSA native leader

<400> 26

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ala Gly Val
1 5 10 15

Ser Gly

<210> 27

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (18)

<223> Variant of HSA native leader

<400> 27

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Gly Val
1 5 10 15

Ser Gly

<210> 28

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (18)

<223> Variant of HSA native leader

<400> 28

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Gly Gly Val
1 5 10 15

Ser Gly

<210> 29

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (14) to (23)

<223> Variant of HSA native leader

<400> 29

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Gly Gly Val

1 5 10 15
 Leu Gly Asp Leu His Lys Ser
 20
 <210> 30
 <211> 22
 <212> PRT
 <213> Artificial Sequence

 <220>
 <221> signal
 <223> Synthetic signal peptide

 <400> 30
 Met Pro Thr Trp Ala Trp Trp Leu Phe Leu Val Leu Leu Ala Leu
 1 5 10 15
 Trp Ala Pro Ala Arg Gly
 20
 <210> 31
 <211> 17
 <212> PRT
 <213> Homo sapiens

 <400> 31
 Met Phe Lys Ser Val Val Tyr Ser Ile Leu Ala Ala Ser Leu Ala Asn
 1 5 10 15
 Ala

 <210> 32
 <211> 29
 <212> PRT
 <213> Homo sapiens

 <400> 32
 Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg
 20 25

 <210> 33
 <211> 23
 <212> PRT
 <213> Homo sapiens

 <400> 33
 Met Lys Leu Ala Tyr Ser Leu Leu Leu Pro Leu Ala Gly Val Ser Ala
 1 5 10 15
 Ser Val Ile Asn Tyr Lys Arg
 20

 <210> 34

<211> 65
 <212> PRT
 <213> Homo sapiens

<400> 34
 Met Lys Leu Lys Thr Val Arg Ser Ala Val Leu Ser Ser Leu Phe Ala
 1 5 10 15
 Ser Gln Val Leu Gly Gln Pro Ile Asp Asp Thr Glu Ser Gln Thr Thr
 20 25 30
 Ser Val Asn Leu Met Ala Asp Asp Thr Glu Ser Ala Phe Ala Thr Gln
 35 40 45
 Thr Asn Ser Gly Gly Leu Asp Val Val Gly Leu Ile Ser Met Ala Lys
 50 55 60
 Arg
 65

<210> 35
 <211> 70
 <212> PRT
 <213> Homo sapiens

<400> 35
 Met Lys Leu Lys Thr Val Arg Ser Ala Val Leu Ser Ser Leu Phe Ala
 1 5 10 15
 Ser Gln Val Leu Gly Gln Pro Ile Asp Asp Thr Glu Ser Gln Thr Thr
 20 25 30
 Ser Val Asn Leu Met Ala Asp Asp Thr Glu Ser Ala Phe Ala Thr Gln
 35 40 45
 Thr Asn Ser Gly Gly Leu Asp Val Val Gly Leu Ile Ser Met Ala Glu
 50 55 60
 Glu Gly Glu Pro Lys Arg
 65 70

<210> 36
 <211> 58
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> primer used to generate XhoI and ClaI
 site in pPPC0006

<400> 36
 gcctcgagaa aagagatgca cacaagagtg aggttgctca tcgatttaaa gatttggg 58

<210> 37

<211> 59
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> primer used in generation XhoI and ClaI
site in pPPC0006

<400> 37
aatcgatgag caacctcact cttgtgtgca tctcttttct cgaggctcct ggaataagc 59

<210> 38
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> primer used in generation XhoI and ClaI
site in pPPC0006

<400> 38
tacaaactta agagtccaat tagc 24

<210> 39
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> primer used in generation XhoI and ClaI
site in pPPC0006

<400> 39
cacttctcta gagggtttc atatgtctt 29

<210> 40
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<221> Misc_Structure
<223> Synthetic oligonucleotide used to alter restriction
sites in pPPC0007

<400> 40
aagctgcctt aggcttataa taaggcgcgc cggccggccg tttaaactaa gcttaattct 60

<210> 41
<211> 60

<212> DNA
<213> Artificial Sequence

<220>
<221> Misc_Structure
<223> Synthetic oligonucleotide used to alter restriction
sites in pPPC0007

<400> 41
agaattaagc ttagtttaaa cggccggccg gcgcgctta ttataagcct aaggcagctt 60

<210> 42
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> forward primer useful for generation of albumin
fusion protein in which the albumin moiety is N-terminal
of the Therapeutic Protein

<220>
<221> misc_feature
<222> (18)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (19)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (20)
<223> n equals a,t,g, or c

<220>
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<222> (21)
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<220>
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<222> (22)
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<220>
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<222> (23)
<223> n equals a,t,g, or c

<220>
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<222> (24)
<223> n equals a,t,g, or c

<220>
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<222> (25)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (26)
<223> n equals a,t,g, or c

<220>
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<222> (27)
<223> n equals a,t,g, or c

<220>
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<222> (28)
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<220>
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<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (30)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (31)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (32)
<223> n equals a,t,g, or c

<400> 42
aagctgcctt aggcttannn nnnnnnnnnn nn

32

<210> 43
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> reverse primer useful for generation of albumin
fusion protein in which the albumin moiety is N-terminal
of the Therapeutic Protein

<220>
<221> misc_feature

<222> (37)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (39)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (40)
<223> n equals a,t,g, or c

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<220>
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<220>
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<222> (45)
<223> n equals a,t,g, or c

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<222> (48)
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<220>
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<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (50)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (51)
<223> n equals a,t,g, or c

<400> 43
gcgcgcgttt aaacggccgg ccggcgcgcc ttattannnn nnnnnnnnnn n

51

<210> 44
<211> 4
<212> PRT
<213> Homo sapiens

<400> 44
Leu Asp Lys Arg
1

<210> 45
<211> 4
<212> PRT
<213> Homo sapiens

<400> 45
Leu Glu Lys Arg
1

<210> 46
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> forward primer useful for generation of albumin fusion
protein in which the albumin moiety is c-terminal of the
Therapeutic Protein

<220>
<221> misc_feature
<222> (19)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (20)
<223> n equals a,t,g, or c

<220>
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<222> (21)
<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (24)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (25)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (26)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (27)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (28)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
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<223> n equals a,t,g, or c

<220>
<221> misc_feature
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<223> n equals a,t,g, or c

<220>

<221> misc_feature
<222> (32)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (33)
<223> n equals a,t,g, or c

<400> 46
aggagcgtcg acaaaagann nnnnnnnnnn nnn

33

<210> 47
<211> 52
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> reverse primer useful for generation of albumin
fusion protein in which the albumin moiety is c-terminal of
the Therapeutic Protein

<220>
<221> misc_feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (39)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (40)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (41)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (42)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (43)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (44)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (45)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (46)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (47)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (48)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (49)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (50)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (51)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (52)

<223> n equals a,t,g, or c

<400> 47

ctttaaatcg atgagcaacc tcactcttgt gtgcacnnn nnnnnnnnnn nn

52

<210> 48

<211> 9

<212> PRT

<213> Homo sapiens

<400> 48

Asp Ala His Lys Ser Glu Val Ala His

1

5

<210> 49

<211> 11

<212> DNA
<213> Artificial Sequence

<220>
<221> misc_feature
<222> (1) to (11)
<223> Kozak sequence

<400> 49
ccgccacccat g

11

<210> 50
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> forward primer useful for inserting Therapeutic
protein into pC4:HSA vector

<220>
<221> misc_feature
<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (30)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (31)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (32)
<223> n equals a,t,g, or c

<220>
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<222> (33)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (34)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (35)
<223> n equals a,t,g, or c

<220>

<221> misc_feature
<222> (36)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (37)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (39)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (40)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (41)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (42)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (43)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (44)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (46)
<223> n equals a,t,g, or c

<400> 50
ccgccgctcg aggggtgtgt ttctgctgann nnnnnnnnnn nnnnnn

<210> 51
<211> 55
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> reverse primer useful for inserting Therapeutic
protein into pC4:HSA vector

<220>
<221> misc_feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (39)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (40)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (41)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (42)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (43)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (44)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (46)
<223> n equals a,t,g, or c

<220>
<221> misc_feature

<222> (47)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (48)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (49)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (50)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (51)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (52)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (53)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (54)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (55)
 <223> n equals a,t,g, or c

<400> 51
 agtcccatcg atgagcaacc tcactcttgt gtgcatcnnn nnnnnnnnnn nnnnn 55

<210> 52
 <211> 733
 <212> DNA
 <213> Homo sapiens

<400> 52
 gggatccgga gcccaaattct tctgacaaaa ctcacacatg cccaccgtgc ccagcacctg 60
 aattcgaggg tgcaccgtca gtcttctctt tcccccaaa acccaaggac accctcatga 120
 tctcccggaac tcctgaggtc acatgcgtgg tgggtggacgt aagccacgaa gaccctgagg 180
 tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca aagccgcggg 240

```

aggagcagta caacagcacg tacctgtgtg tcagcgtcct caccgtcctg caccaggact 300
ggctgaatgg caaggagtag aagtgcagg tctccaacaa agccctccca acccccatcg 360
agaaaacccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac accctgcccc 420
catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctgggc aaaggcttct 480
atccaagcga catcgccgtg gagggggaga gcaatgggca gccggagaac aactacaaga 540
ccacgcctcc cgtgctggac tccgacggct ccttcttctc ctacagcaag ctcaccgtgg 600
acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggctctgc 660
acaaccacta caccgagaag agcctctccc tgtctccggg taaatgagtg cgacggccgc 720
gactctagag gat 733

```

<210> 53

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<221> Site

<222> (3)

<223> Xaa equals any of the twenty naturally occurring L-amino acids

<400> 53

Trp Ser Xaa Trp Ser

1

5

<210> 54

<211> 86

<212> DNA

<213> Artificial Sequence

<220>

<221> Primer_Bind

<223> Synthetic sequence with 4 tandem copies of the GAS binding site found in the IRF1 promoter (Rothman et al., Immunity 1:457-468 (1994)), 18 nucleotides complementary to the SV40 early promoter, and a Xho I restriction site.

<400> 54

```

gcgcctcgag atttccccga aatctagatt tccccgaaat gatttccccg aaatgatttc 60
cccgaaatat ctgccatctc aattag 86

```

<210> 55

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<221> Primer_Bind

<223> Synthetic sequence complementary to the SV40 promoter; includes a Hind III restriction site.

<400> 55

gcggcaagct ttttgcaaag cctaggc

27

<210> 56

<211> 271

<212> DNA

<213> Artificial Sequence

<220>

<221> Protein_Bind

<223> Synthetic promoter for use in biological assays; includes GAS binding sites found in the IRF1 promoter

<400> 56

```

ctcgagattt ccccgaaatc tagatttccc cgaaatgatt tccccgaaat gatttccccg      60
aaatatctgc catctcaatt agtcagcaac catagtcccc cccctaactc cgcccatccc      120
gccctaact cgcgccagtt ccgcccattc tccgccccat ggctgactaa ttttttttat      180
ttatgcagag gccgaggccg cctcggcctc tgagctattc cagaagtagt gaggaggctt      240
ttttggaggc ctaggctttt gcaaaaagct t                                     271

```

<210> 57

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<221> Primer_Bind

<223> Synthetic primer complementary to human genomic EGR-1 promoter sequence; includes a Xho I restriction site.

<400> 57

```

gcgctcgagg gatgacagcg atagaacccc gg                                     32

```

<210> 58

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<221> Primer_Bind

<223> Synthetic primer complementary to human genomic EGR-1 promoter sequence; includes a Hind III restriction site.

<400> 58

```

gcgaagcttc gcgactcccc ggatccgcct c                                     31

```

<210> 59

<211> 12

<212> DNA

<213> Homo sapiens

<400> 59

```

ggggactttc cc                                                         12

```

<210> 60

<211> 73

<212> DNA

<213> Artificial Sequence

<220>

<221> Primer_Bind

<223> Synthetic primer with 4 tandem copies of the NF-KB binding site (GGGGACTTCCCC), 18 nucleotides complementary to the 5' end of the SV40 early promoter sequence, and a XhoI restriction site.

<400> 60
 gcggcctcga ggggactttc ccggggactt tccggggact ttccgggact ttccatcctg 60
 ccattctcaat tag 73

<210> 61
 <211> 256
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> Protein_Bind
 <223> Synthetic promoter for use in biological assays; includes NF-KB binding sites.

<400> 61
 ctcgagggga ctttcccggg gactttccgg ggactttccg ggactttcca tctgccatct 60
 caattagtca gcaaccatag tcccggccct aactccgccc atcccggccc taactccgcc 120
 cagttccgcc cattctccgc cccatggctg actaattttt tttatttatg cagaggccga 180
 ggccgcctcg gcctctgagc tattccagaa gtagtgagga ggcttttttg gaggcctagg 240
 cttttgcaaa aagctt 256

<210> 62
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> Degenerate VH forward primer useful for amplifying human VH domains

<400> 62
 caggtgcagc tgggtgcagtc tgg 23

<210> 63
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> Degenerate VH forward primer useful for amplifying human VH domains

<400> 63
 caggtcaact taaggagtc tgg 23

<210> 64
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind

<223> Degenerate VH forward primer useful for amplifying human VH domains

<400> 64

gaggtgcagc tgggtggagtc tgg

23

<210> 65

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate VH forward primer useful for amplifying human VH domains

<400> 65

caggtgcagc tgcaggagtc ggg

23

<210> 66

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate VH forward primer useful for amplifying human VH domains

<400> 66

gaggtgcagc tgttgcagtc tgc

23

<210> 67

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate VH forward primer useful for amplifying human VH domains

<400> 67

caggtacagc tgcagcagtc agg

23

<210> 68

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate JH reverse primer useful for amplifying human VH domains

<400> 68
tgaggagacg gtgaccaggg tgcc 24

<210> 69
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate JH reverse primer useful for
amplifying human VH domains

<400> 69
tgaagagacg gtgaccattg tccc 24

<210> 70
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate JH reverse primer useful for
amplifying human VH domains

<400> 70
tgaggagacg gtgaccaggg ttcc 24

<210> 71
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate JH reverse primer useful for
amplifying human VH domains

<400> 71
tgaggagacg gtgaccgtgg tccc 24

<210> 72
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 72
gacatccaga tgaccagtc tcc 23

<210> 73
<211> 23

<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 73
gatgttgtga tgactcagtc tcc 23

<210> 74
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 74
gatattgtga tgactcagtc tcc 23

<210> 75
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 75
gaaattgtgt tgacgcagtc tcc 23

<210> 76
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 76
gacatcgtga tgaccagtc tcc 23

<210> 77
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind

<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 77

gaaacgacac tcacgcagtc tcc

23

<210> 78

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate Vkappa forward primer useful for
amplifying human VL domains

<400> 78

gaaattgtgc tgactcagtc tcc

23

<210> 79

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate Vlamba forward primer useful for
amplifying human VL domains

<400> 79

cagtctgtgt tgacgcagcc gcc

23

<210> 80

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate Vlamba forward primer useful for
amplifying human VL domains

<400> 80

cagtctgccc tgactcagcc tgc

23

<210> 81

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<221> primer_bind

<223> Degenerate Vlamba forward primer useful for
amplifying human VL domains

<400> 81

tcctatgtgc tgactcagcc acc

23

<210> 82
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vlambda forward primer useful for
amplifying human VL domains

<400> 82
tcttctgagc tgactcagga ccc

23

<210> 83
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vlambda forward primer useful for
amplifying human VL domains

<400> 83
cacgttatac tgactcaacc gcc

23

<210> 84
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vlambda forward primer useful for
amplifying human VL domains

<400> 84
caggctgtgc tcactcagcc gtc

23

<210> 85
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Vlambda forward primer useful for
amplifying human VL domains

<400> 85
aattttatgc tgactcagcc cca

23

<210> 86
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jkappa reverse primer useful for
amplifying human VL domains

<400> 86
acgttttgatt tccaccttgg tccc

24

<210> 87
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jkappa reverse primer useful for
amplifying human VL domains

<400> 87
acgtttgatc tccagcttgg tccc

24

<210> 88
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jkappa reverse primer useful for
amplifying human VL domains

<400> 88
acgttttgata tccactttgg tccc

24

<210> 89
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jkappa reverse primer useful for
amplifying human VL domains

<400> 89
acgttttgatc tccaccttgg tccc

24

<210> 90
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jkappa reverse primer useful for
amplifying human VL domains

<400> 90
acgtttaatc tccagtcgtg tccc 24

<210> 91
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jlambda reverse primer useful for
amplifying human VL domains

<400> 91
cagtctgtgt tgacgcagcc gcc 23

<210> 92
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jlambda reverse primer useful for
amplifying human VL domains

<400> 92
cagtctgccc tgactcagcc tgc 23

<210> 93
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jlambda reverse primer useful for
amplifying human VL domains

<400> 93
tcctatgtgc tgactcagcc acc 23

<210> 94
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> Degenerate Jlambda reverse primer useful for
amplifying human VL domains

<400> 94
tcttctgagc tgactcagga ccc 23

<210> 95

<211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> Degenerate Jlambda reverse primer useful for
 amplifying human VL domains

<400> 95
 cacgttatac tgactcaacc gcc

23

<210> 96
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> Degenerate Jlambda reverse primer useful for
 amplifying human VL domains

<400> 96
 caggctgtgc tcactcagcc gtc

23

<210> 97
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> Degenerate Jlambda reverse primer useful for
 amplifying human VL domains

<400> 97
 aattttatgc tgactcagcc cca

23

<210> 98
 <211> 5
 <212> PRT
 <213> Homo sapiens

<400> 98
 Cys Asp Leu Pro Gln
 1 5

<210> 99
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 99
 Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Thr Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp Leu
 65 70 75 80
 Leu Asp Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met Asn
 100 105 110
 Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr Leu
 115 120 125
 Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu Arg
 145 150 155 160
 Leu Arg Arg Lys Glu
 165

<210> 100
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 100
 Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met Asn
 100 105 110

Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr Leu
115 120 125

Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140

Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu Arg
145 150 155 160

Leu Arg Arg Lys Glu
165

<210> 101

<211> 165

<212> PRT

<213> Homo sapiens

<400> 101

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Met Glu
85 90 95

Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met Asn
100 105 110

Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125

Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Lys Ile Phe Gln Glu Arg
145 150 155 160

Leu Arg Arg Lys Glu
165

<210> 102

<211> 165

<212> PRT

<213> Homo sapiens

<400> 102

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met Tyr
 100 105 110
 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125
 Tyr Leu Thr Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Ile Asn Leu Gln Lys Arg
 145 150 155 160
 Leu Lys Ser Lys Glu
 165

<210> 103

<211> 167

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (115)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 103

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ala Ala Trp Asp Glu

41

165

<210> 105
 <211> 48
 <212> DNA
 <213> Artificial sequence

<220>
 <221> primer_bind
 <223> primer for BNP amplification, has BamHI cloning site

<400> 105
 ccgccgctcg aggggtgtgt ttcgtcgaag cccaagatg gtgcaagg 48

<210> 106
 <211> 57
 <212> DNA
 <213> Artificial sequence

<220>
 <221> primer_bind
 <223> primer for BNP amplification, has ClaI cloning site

<400> 106
 agtccccatcg atgagcaacc tactcttgt gtgcatcatg ccgcctcagc actttgc 57

<210> 107
 <211> 106
 <212> DNA
 <213> Artificial sequence

<220>
 <221> primer_bind
 <223> primer for full-length IFN γ amplification, has BamHI cloning site

<400> 107
 gcgcggatcc gaattccgcc gccatgacca acaagtgtct cctccaaatt gctctcctgt 60
 tgtgtctctc cactacagct cttccatga gctacaactt gcttgg 106

<210> 108
 <211> 55
 <212> DNA
 <213> Artificial sequence

<220>
 <221> primer_bind
 <223> primer for full-length IFN γ amplification, has ClaI cloning site

<400> 108
 gcgcgcatcg atgagcaacc tactcttgt gtgcatcggt tcggaggtaa cctgt 55

<210> 109
 <211> 41
 <212> DNA
 <213> Homo sapiens

<400> 109
cgcgcgcgctc gacaaaagat gtgatctgcc tcaaaccac a 41

<210> 110
<211> 59
<212> DNA
<213> Homo sapiens

<400> 110
gcgcgcacgc atgagcaacc tcactcttgt gtgcattctt cttacttctt aaactttct 59

<210> 111
<211> 204
<212> DNA
<213> Homo sapiens

<400> 111
tcacggggac cttaccaccc ctgagagtgc tgcttcacct acactaccta caagatcccg 60
cgtcagagaa ttatggatta ctatgagacc aacagccagt gctccaagcc cggaattgtc 120
ttcatcacca aaaggggcca ttccgtctgt accaacccca gtgacaagtg ggtccaggac 180
tatatcaagg acatgaagga gaac 204

<210> 112
<211> 204
<212> DNA
<213> Homo sapiens

<400> 112
tcacggggac cttaccaccc ctgagagtgc tgcttcacct acactaccta caagatcccg 60
cgtcagagaa ttatggatta ctatgagacc aacagccagt gctccaagcc cggaattgtc 120
ttcatcacca aaaggggcca ttccgtctgt accaacccca gtgacaagtg ggtccaggac 180
tatatcaagg acatgaagga gaac 204

<210> 113
<211> 198
<212> DNA
<213> Homo sapiens

<400> 113
ggaccttacc acccctcaga gtgctgcttc acctaccta cctacaagat cccgcgtcag 60
agaattatgg attactatga gaccaacagc cagtgtctca agcccggaa tgtcttcac 120
accaaaaggg gccattccgt ctgtaccaac cccagtgcac agtgggtcca ggactatata 180
aaggacatga aggagaac 198

<210> 114
<211> 96
<212> DNA
<213> Homo sapiens

<400> 114
agccccaaga tgggtgcaagg gtctggctgc tttgggagga agatggaccg gatcagctcc 60
tccagtggcc tgggctgcaa agtgctgagg cggcat 96

<210> 115
<211> 726
<212> DNA

<213> Homo sapiens

<400> 115

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gccaccatgg tgagcaaggg cgaggagctg ttcaccgggg tggtgcccat cctggtcgag 60
ctggacggcg acgtaaaccg ccacaagttc agcgtgtccg gcgagggcga gggcgatgcc 120
acctacggca agctgacctt gaagttcatc tgcaccaccg gcaagctgcc cgtgccctgg 180
cccaccctcg tgaccacctt gacctacggc gtgcagtgtc tcagccgcta ccccgaccac 240
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aaccactacc tgagcaccca gtccgcctcg agcaaagacc ccaacgagaa gcgcgatcac 660
atggtcctgc tggagtctgt gaccgcgccg gggatcactc tcggcatgga cgagctgtac 720
aagtaa 726

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<210> 116

<211> 495

<212> DNA

<213> Homo sapiens

<400> 116

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gaggagtgtt gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
cagcagatct tcaatctctt cagcacaaag gactcatctg ctgcttgagg tgagaccctc 240
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caggggggtg ggggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg 360
aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg 420
gaggttgtca gagcagaaat catgagatct ttttctttgt caacaaactt gcaagaaagt 480
ttaagaagta aggaa 495

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<210> 117

<211> 495

<212> DNA

<213> Homo sapiens

<400> 117

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tgtgatctgc ctcaaaccce cagcctgggt tctagaagga ccttgatgct cctggcacag 60
atgaggagaa tctctctttt ctctgtcttg aaggacagac atgacttttg atttccccag 120
gaggagtgtt gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
cagcagatct tcaatctctt cagcacaaag gactcatctg ctgcttgagg tgagaccctc 240
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caggggggtg ggggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg 360
aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg 420
gaggttgtca gagcagaaat catgagatct ttttctttgt caacaaactt gcaagaaagt 480
ttaagaagta aggaa 495

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<210> 118

<211> 495

<212> DNA

<213> Homo sapiens

<400> 118

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tgtgatctgc ctcaaaccac cagcctgggt tctagaagga ccttgatgct cctggcacag 60
atgaggagaa tctctctttt ctctgcttg aaggacagac atgactttgg atttccccag 120
gaggagtgtg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttgga tgagaccctc 240
ctagacaaat tctacactga actctaccag cagctgaatg acctggaagc ctgtgtgata 300
cagggggtgg ggggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg 360
aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg 420
gaggttgtca gacagaaat catgagatct ttttcttgt caacaaactt gcaagaaagt 480
ttaagaagta aggaa 495

```

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<210> 119
<211> 90
<212> DNA
<213> Homo sapiens

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```

<400> 119
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggg taagggtaga 90

```

```

<210> 120
<211> 42
<212> DNA
<213> Homo sapiens

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```

<400> 120
gctggttgta agaacttctt ctggaagact ttcacttctt gt 42

```

```

<210> 121
<211> 90
<212> DNA
<213> Homo sapiens

```

```

<400> 121
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggg taagggtaga 90

```

```

<210> 122
<211> 90
<212> DNA
<213> Homo sapiens

```

```

<400> 122
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggg taagggtaga 90

```

```

<210> 123
<211> 90
<212> DNA
<213> Homo sapiens

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<400> 123
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggg taagggtaga 90

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<210> 124
<211> 96
<212> DNA
<213> Homo sapiens

<400> 124
agccccaaga tgggtgcaagg gtctggctgc tttgggagga agatggaccg gatcagctcc 60
tccagtggcc tgggctgcaa agtgctgagg cggcat 96

<210> 125
<211> 90
<212> DNA
<213> Homo sapiens

<400> 125
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggt taagggtaga 90

<210> 126
<211> 90
<212> DNA
<213> Homo sapiens

<400> 126
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gaattcattg cttggttggt taagggtaga 90

<210> 127
<211> 90
<212> DNA
<213> Homo sapiens

<400> 127
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggt taagggtaga 90

<210> 128
<211> 90
<212> DNA
<213> Homo sapiens

<400> 128
cacggtgaag gtactttcac ttctgatgtt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggt taagggtaga 90

<210> 129
<211> 90
<212> DNA
<213> Homo sapiens

<400> 129
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gaattcattg cttggttggt taagggtaga 90

<210> 130
<211> 96
<212> DNA
<213> Homo sapiens

<400> 130
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tccagtggcc tgggctgcaa agtgctgagg cggcat 96

<210> 131
<211> 90
<212> DNA
<213> Homo sapiens

<400> 131
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gaattcattg cttggttggt taagggtaga 90

<210> 132
<211> 90
<212> DNA
<213> Homo sapiens

<400> 132
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gaattcattg cttggttggt taagggtaga 90

<210> 133
<211> 90
<212> DNA
<213> Homo sapiens

<400> 133
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gaattcattg cttggttggt taagggtaga 90

<210> 134
<211> 90
<212> DNA
<213> Homo sapiens

<400> 134
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gaattcattg cttggttggt taagggtaga 90

<210> 135
<211> 84
<212> DNA
<213> Homo sapiens

<400> 135
agcctgcgga gatccagctg cttcgggggc aggatggaca ggattggagc ccagagcgga 60
ctgggctgta acagcttccg gtac 84

<210> 136
<211> 90
<212> DNA
<213> Homo sapiens

<400> 136
cacggtgaag gtactttcac ttctgatggt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggt taagggtaga 90

<210> 137
<211> 90
<212> DNA
<213> Homo sapiens

<400> 137
cacggtgaag gtactttcac ttctgatggt tcttcttact tggaaggta agctgctaag 60
gaattcattg cttggttggt taagggtaga 90

<210> 138
<211> 90
<212> DNA
<213> Homo sapiens

<400> 138
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gaattcattg cttggttggt taagggtaga 90

<210> 139
<211> 102
<212> DNA
<213> Homo sapiens

<400> 139
atcaaaccg aggctcccg cgaagacgc tcgccggagg agctgaaccg ctactacgcc 60
tccctgcgcc actacactcaa cctgggcacc cggcagcgg at 102

<210> 140
<211> 87
<212> DNA
<213> Homo sapiens

<400> 140
agccccaaga tgggtgaagg gtctggctgc tttgggagga agatggaccg gatcagctcc 60
tccagtggcc tgggctgcaa agtgctg 87

<210> 141
<211> 87
<212> DNA
<213> Homo sapiens

<400> 141

agccccaaga tgggtgcaagg gtctggctgc tttgggagga agatggaccg gatcagctcc 60
tccagtggcc tgggctgcaa agtgctg 87

<210> 142

<211> 102

<212> DNA

<213> Homo sapiens

<400> 142

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tccctgcgcc actacctcaa cctggtcacc cggcagcggg at 102

<210> 143

<211> 96

<212> DNA

<213> Homo sapiens

<400> 143

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tccagtggcc tgggctgcaa agtgctgagg cggcat 96

<210> 144

<211> 96

<212> DNA

<213> Homo sapiens

<400> 144

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tccagtggcc tgggctgcaa agtgctgagg cggcat 96

<210> 145

<211> 99

<212> DNA

<213> Homo sapiens

<400> 145

catgctgatg gttctttctc tgatgagatg aacaccattc ttgataatct tgccgccagg 60
gactttataa actggttgat tcagaccaa atcactgac 99

<210> 146

<211> 99

<212> DNA

<213> Homo sapiens

<400> 146

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gactttataa actggttgat tcagaccaa atcactgac 99

<210> 147

<211> 78

<212> DNA

<213> Homo sapiens

<400> 147

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tccagtggcc tgggctgc 78

<210> 148
 <211> 81
 <212> DNA
 <213> Homo sapiens

<400> 148
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 tccagtggcc tgggctgcaa a 81

<210> 149
 <211> 84
 <212> DNA
 <213> Homo sapiens

<400> 149
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 tccagtggcc tgggctgcaa agtg 84

<210> 150
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 <212> DNA
 <213> Homo sapiens

<400> 150
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 gactttataa actggttgat tcagaccaa atcactgac 99

<210> 151
 <211> 99
 <212> DNA
 <213> Homo sapiens

<400> 151
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 gactttataa actggttgat tcagaccaa atcactgac 99

<210> 152
 <211> 81
 <212> DNA
 <213> Homo sapiens

<400> 152
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 aaatacttgg cggccgtcct a 81

<210> 153
 <211> 81
 <212> DNA
 <213> Homo sapiens

<400> 153
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 aaatacttgg cggccgtcct a 81

<210> 154

<211> 114
 <212> DNA
 <213> Homo sapiens

<400> 154
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 aaatacttgg cgcccgctcct aggggaagagg tataaacaaa ggggttaaaaa caaa 114

<210> 155
 <211> 114
 <212> DNA
 <213> Homo sapiens

<400> 155
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 aaatacttgg cgcccgctcct aggggaagagg tataaacaaa ggggttaaaaa caaa 114

<210> 156
 <211> 357
 <212> DNA
 <213> Homo sapiens

<400> 156
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 acggcggcag acaaaaagac tgcagtggac atgtcgggcg ggacgggtcac agtccttgaa 120
 aaggctccctg tatcaaaaagg ccaactgaag caatacttct acgagaccaa gtgcaatccc 180
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 cgaactaccc agtcgtacgt gcggggccctt accatggata gcaaaaagag aattggctgg 300
 cgattcataa ggatagacac ttcttgtgta tgtacattga ccattaaaag gggaaga 357

<210> 157
 <211> 357
 <212> DNA
 <213> Homo sapiens

<400> 157
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 acggcggcag acaaaaagac tgcagtggac atgtcgggcg ggacgggtcac agtccttgaa 120
 aaggctccctg tatcaaaaagg ccaactgaag caatacttct acgagaccaa gtgcaatccc 180
 atgggttaca caaaagaagg ctgcaggggc atagacaaaa ggcatgggaa ctcccagtcg 240
 cgaactaccc agtcgtacgt gcggggccctt accatggata gcaaaaagag aattggctgg 300
 cgattcataa ggatagacac ttcttgtgta tgtacattga ccattaaaag gggaaga 357

<210> 158
 <211> 357
 <212> DNA
 <213> Homo sapiens

<400> 158
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 aaggctccctg tatcaaaaagg ccaactgaag caatacttct acgagaccaa gtgcaatccc 180
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 cgattcataa ggatagacac ttcttgtgta tgtacattga ccattaaaag gggaaga 357

<210> 159

<211> 357
 <212> DNA
 <213> Homo sapiens

<400> 159
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 aaggctccctg tatcaaaagg ccaactgaag caatacttct acgagaccaa gtgcaatccc 180
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 cgaactaccc agtcgtacgt gcggggccctt accatggata gcaaaaagag aattggctgg 300
 cgattcataa ggatagacac ttcttgtgta tgtacattga ccattaaaag gggaaga 357

<210> 160
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 <212> DNA
 <213> Homo sapiens

<400> 160
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 aaggctccctg tatcaaaagg ccaactgaag caatacttct acgagaccaa gtgcaatccc 180
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 cgaactaccc agtcgtacgt gcggggccctt accatggata gcaaaaagag aattggctgg 300
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<210> 161
 <211> 357
 <212> DNA
 <213> Homo sapiens

<400> 161
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 aaggctccctg tatcaaaagg ccaactgaag caatacttct acgagaccaa gtgcaatccc 180
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 cgaactaccc agtcgtacgt gcggggccctt accatggata gcaaaaagag aattggctgg 300
 cgattcataa ggatagacac ttcttgtgta tgtacattga ccattaaaag gggaaga 357

<210> 162
 <211> 579
 <212> DNA
 <213> Homo sapiens

<400> 162
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 cgccgcgcgc cgcccttcgc gctgagcagt gactcaaata tgccagagga ttatcctgat 120
 cagttcgatg atgtcatgga tttttattcaa gccaccatta aaagactgaa aagggtcacca 180
 gataaacaaa tggcagtgtc tcctagaaga gagcggaatc ggcagggtgc agctgccaac 240
 ccagagaatt ccagaggaaa aggtcggaga ggccagaggg gcaaaaaccg gggttgtgtc 300
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 ctgattttta ggtactgcag cggctcttgc gatgcagctg agacaacgta cgacaaaata 420
 ttgaaaaaact tatccagaaa tagaaggctg gtgagtgaca aagtagggca ggcattgttc 480
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 ctaagaaagc attccgctaa aagggtgtgga tgtatctga 579

<210> 163
 <211> 579

<212> DNA

<213> Homo sapiens

<400> 163

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cgccgccgcg	cgcccttcgc	gctgagcagt	gactcaaata	tgccagagga	ttatcctgat	120
cagttcgatg	atgtcatgga	ttttattcaa	gccaccatta	aaagactgaa	aaggtcacca	180
gataaacaaa	tggcagtgtc	tcctagaaga	gagcggaatc	ggcaggctgc	agctgccaac	240
ccagagaatt	ccagaggaaa	aggtcggaga	ggccagaggg	gcaaaaaccg	gggttgtgtc	300
ttaactgcaa	tacatttaaa	tgctactgac	ttgggtctgg	gctatgaaac	caaggaggaa	360
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ttgaaaaact	tatccagaaa	tagaaggctg	gtgagtgaca	aagtagggca	ggcatgttgc	480
agacccatcg	cctttgatga	tgacctgtcg	tttttagatg	ataacctggt	ttaccatatt	540
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<210> 164

<211> 306

<212> DNA

<213> Homo sapiens

<400> 164

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ggcctgggct	acgcgtccga	cgagacgggtg	ctgttccgct	actgcgcagg	cgcttgcgag	120
gctgccgcgc	gcgtctacga	cctcgggctg	cgacgactgc	gccagcggcg	gcgcctgcgg	180
cgggagcggg	tgccgcgcga	gccctgtctg	cgcccagcgg	cctacgagga	cgaggtgtcc	240
ttcctggacg	cgcacagccg	ctaccacacg	gtgcacgagc	tgctggcgcg	cgagtgcgcc	300
tgcggtg						306

<210> 165

<211> 306

<212> DNA

<213> Homo sapiens

<400> 165

gcgcggttgg	gggcgcggcc	ttgcgggctg	cgcgagctgg	aggtgcgcgt	gagcgagctg	60
ggcctgggct	acgcgtccga	cgagacgggtg	ctgttccgct	actgcgcagg	cgcttgcgag	120
gctgccgcgc	gcgtctacga	cctcgggctg	cgacgactgc	gccagcggcg	gcgcctgcgg	180
cgggagcggg	tgccgcgcga	gccctgtctg	cgcccagcgg	cctacgagga	cgaggtgtcc	240
ttcctggacg	cgcacagccg	ctaccacacg	gtgcacgagc	tgctggcgcg	cgagtgcgcc	300
tgcggtg						306

<210> 166

<211> 357

<212> DNA

<213> Homo sapiens

<400> 166

tacgcggagc	ataagagtca	ccgaggggag	tactcggtat	gtgacagtga	gagtctgtgg	60
gtgaccgaca	agtcacggc	catcgacatt	cggggacacc	aggtcacggt	gctgggggag	120
atcaaaacgg	gcaactctcc	cgtcaaacaa	tatttttatg	aaacgcgatg	taaggaagcc	180
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acatcccaaa	cctacgtccg	agcactgact	tcagagaaca	ataaaactcg	gggctggcgg	300
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<210> 167

<211> 357

<212> DNA

<213> Homo sapiens

<400> 167

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gtg	ac	cg	ga	ag	tc	at	cg	gc	cat	cg	ac	att	cg	gg	gg	ac	acc	agg	tc	ac	gg	t	g	ct	gg	120
atc	aaa	ac	cg	gca	act	ct	cc	cg	tca	aa	aca	aa	tatt	tt	t	at	g	aa	ac	gc	gat	t	a	ag	ga	180
agg	cc	gg	tca	aaa	ac	gg	tt	t	g	gg	gg	tatt	gat	gata	aa	ac	act	gga	act	c	t	ag	t	g	caa	240
aca	tcc	ca	aaa	cct	ac	gt	cc	g	ag	ca	ct	gact	tc	aga	ga	aca	ata	aa	act	cg	t	g	g	ct	gg	300
tgg	ata	cg	ga	tag	ac	ac	gt	c	ct	gt	gt	gt	gc	ct	t	g	ca	aa	at	cg	t	a	g	a	aca	357

<210> 168

<211> 405

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<400> 168

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ctg	t	ct	gg	t	cat	g	cc	ag	ct	g	tg	g	ag	cc	t	g	tc	cg	t	gg	c	ag	ag	ct	gg	180
tac	g	cc	ct	cag	agg	aga	a	agg	t	cat	ct	t	cc	gc	t	act	g	c	gc	cg	g	c	ag	ct	g	240
cg	a	ccc	cag	at	g	cc	ct	gg	g	g	ct	gg	cc	cg	ct	g	cag	gg	cc	agg	g	c	c	ac	g	300
cc	t	g	ct	g	cc	cc	act	cg	ct	a	c	ac	cc	g	ac	gt	g	gc	ct	t	cc	tc	g	at	g	360
cag	cg	g	ct	g	c	c	ag	ct	ct	c	g	g	g	g	ct	g	g	g	ct	g	g	t	g	g	c	405

<210> 169

<211> 405

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ctg	t	ct	gg	t	cat	g	cc	ag	ct	g	tg	g	ag	cc	t	g	tc	cg	t	gg	c	ag	ag	ct	gg	180
tac	g	cc	ct	cag	agg	aga	a	agg	t	cat	ct	t	cc	gc	t	act	g	c	gc	cg	g	c	ag	ct	g	240
cg	a	ccc	cag	at	g	cc	ct	gg	g	g	ct	gg	cc	cg	ct	g	cag	gg	cc	agg	g	c	c	ac	g	300
cc	t	g	ct	g	cc	cc	act	cg	ct	a	c	ac	cc	g	ac	gt	g	gc	ct	t	cc	tc	g	at	g	360
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<210> 170

<211> 543

<212> DNA

<213> Homo sapiens

<400> 170

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cg	g	cc	g	cc	gc	ct	tc	cg	cc	cg	cg	cc	cc	cc	g	cc	gc	cc	cc	at	ct	g	ct	ct	t	180	
cccc	g	cg	gg	gg	g	cc	g	cg	gg	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	240	
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cg	ct	cc	g	ac	g	ct	gg	t	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	360	
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tc	cc	g	g	cc	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	g	480	
gac	gt	ca	aca	gc	ac	ct	gg	ag	aa	cc	gt	gg	ac	gc	ct	ct	cc	g	cc	ac	gc	ct	g	g	ct	540	
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<400> 171

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cggccgcgc	cgcagccttc	tcggcccgcg	ccccgcgcgc	ctgcaccccc	atctgctctt	180
ccccgcggg	gccgcgcggc	gcgggctggg	ggcccgggca	gccgcgctcg	ggcagcgggg	240
gcgcggggct	gccgcctgcg	ctcgcagctg	gtgccgggtg	gcgcgctcgg	cctggggccac	300
cgctccgacg	agctgggtgcg	tttccgcttc	tgcagcggct	cctgccgcgcg	cgcgcgctct	360
ccacacgacc	tcagcctggc	cagcctactg	ggcgccgggg	ccctgcgacc	gcccccgggc	420
tcccgccccg	tcagccagcc	ctgctgccga	cccacgcgct	acgaagcgg	ctccttcacg	480
gacgtcaaca	gcacctggag	aaccgtggac	cgcctctccg	ccaccgcctg	cggctgcctg	540
ggc						543

<210> 172

<211> 543

<212> DNA

<213> Homo sapiens

<400> 172

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cggccgcgc	cgcagccttc	tcggcccgcg	ccccgcgcgc	ctgcaccccc	atctgctctt	180
ccccgcggg	gccgcgcggc	gcgggctggg	ggcccgggca	gccgcgctcg	ggcagcgggg	240
gcgcggggct	gccgcctgcg	ctcgcagctg	gtgccgggtg	gcgcgctcgg	cctggggccac	300
cgctccgacg	agctgggtgcg	tttccgcttc	tgcagcggct	cctgccgcgcg	cgcgcgctct	360
ccacacgacc	tcagcctggc	cagcctactg	ggcgccgggg	ccctgcgacc	gcccccgggc	420
tcccgccccg	tcagccagcc	ctgctgccga	cccacgcgct	acgaagcgg	ctccttcacg	480
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ggc						543

<210> 173

<211> 543

<212> DNA

<213> Homo sapiens

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cggccgcgc	cgcagccttc	tcggcccgcg	ccccgcgcgc	ctgcaccccc	atctgctctt	180
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<210> 174

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cggcgcgcgc	cgcagccttc	tcggcccgcg	ccccgcgcgc	ctgcaccccc	atctgctctt	180
ccccgcgggg	gccgcgcggc	gcgggctggg	ggccccggga	gccgcgctcg	ggcagcgggg	240
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tcccgcccg	tcagccagcc	ctgctgccga	cccacgcgct	acgaagcggg	ctccttcattg	480
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<212> DNA

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cggcgcgcgc	cgcagccttc	tcggcccgcg	ccccgcgcgc	ctgcaccccc	atctgctctt	180
ccccgcgggg	gccgcgcggc	gcgggctggg	ggccccggga	gccgcgctcg	ggcagcgggg	240
gcgcggggct	gccgcctgcg	ctcgcagctg	gtgccggtgc	gcgcgctcgg	cctggggccac	300
cgctccgacg	agctggtgcg	tttccgcttc	tgcagcggct	cctgccgcgc	cgcgcgctct	360
ccacacgacc	tcagcctggc	cagcctactg	ggcgccgggg	ccctgcgacc	gccccggggc	420
tcccgcccg	tcagccagcc	ctgctgccga	cccacgcgct	acgaagcggg	ctccttcattg	480
gacgtcaaca	gcacctggag	aaccgtggac	cgcctctccg	ccaccgcctg	cggctgcctg	540
ggc						543

<210> 176

<211> 390

<212> DNA

<213> Homo sapiens

<400> 176

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gtggacagga	ggcactgggt	atctgagtg	aaggccaagc	agtcctatgt	gcgggcattg	300
accgctgatg	cccagggccg	tgtgggctgg	cgatggattc	gaattgacac	tgcctgcgtc	360
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<212> DNA

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gtggacagga	ggcactgggt	atctgagtg	aaggccaagc	agtcctatgt	gcgggcattg	300
accgctgatg	cccagggccg	tgtgggctgg	cgatggattc	gaattgacac	tgcctgcgtc	360
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<210> 178

<211> 84

<212> DNA

<213> Homo sapiens

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aaatatttga actcaattct gaat 84

<210> 179

<211> 84

<212> DNA

<213> Homo sapiens

<400> 179

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aaatatttga actcaattct gaat 84

<210> 180

<211> 81

<212> DNA

<213> Homo sapiens

<400> 180

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cggctgctac agggcctggt g 81

<210> 181

<211> 81

<212> DNA

<213> Homo sapiens

<400> 181

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cggctgctac agggcctggt g 81

<210> 182

<211> 360

<212> DNA

<213> Homo sapiens

<400> 182

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gaggtgaaca ttaacaacag tgtattcaaa cagtactttt ttgagaccaa gtgccgggac 180
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accacgactc acacctttgt caaggcgctg accatggatg gcaagcaggc tgcctggcgg 300
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<211> 360

<212> DNA

<213> Homo sapiens

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gaggtgaaca ttaacaacag tgtattcaaa cagtactttt ttgagaccaa gtgccgggac 180
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<212> DNA

<213> Homo sapiens

<400> 189

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aagtaccttg agtctcttat g 81

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<211> 81

<212> DNA

<213> Homo sapiens

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agctgcgcct gggtg 75

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<211> 75

<212> DNA

<213> Homo sapiens

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agctgcgcct gggtg 75

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<211> 156

<212> DNA

<213> Homo sapiens

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atggaccgga tcagctcctc cagtggcctg ggctgc 156

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<211> 84

<212> DNA

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<210> 196

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 20 25 30

Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg Ile Met Asp Tyr Tyr Glu
 35 40 45

Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile Val Phe Ile Thr Lys Arg
 50 55 60

Gly His Ser Val Cys Thr Asn Pro Ser Asp Lys Trp Val Gln Asp Tyr
 65 70 75 80

Ile Lys Asp Met Lys Glu Asn Asp Ala His Lys Ser Glu Val Ala His
 85 90 95

Arg Phe Lys Asp Leu Gly Glu Asp Ala His Lys Ser Glu Val Ala His
 100 105 110

Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile
 115 120 125

Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
 130 135 140
 Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
 145 150 155 160
 Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
 165 170 175
 Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp
 180 185 190
 Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
 195 200 205
 Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp
 210 215 220
 Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys
 225 230 235 240
 Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
 245 250 255
 Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys
 260 265 270
 Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu
 275 280 285
 Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala
 290 295 300
 Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
 305 310 315 320
 Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys
 325 330 335
 Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp
 340 345 350
 Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys
 355 360 365
 Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys
 370 375 380
 Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu
 385 390 395 400
 Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys
 405 410 415
 Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met
 420 425 430

Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu
 435 440 445
 Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys
 450 455 460
 Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe
 465 470 475 480
 Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
 485 490 495
 Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
 500 505 510
 Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
 515 520 525
 Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
 530 535 540
 Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
 545 550 555 560
 Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
 565 570 575
 Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
 580 585 590
 Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
 595 600 605
 Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
 610 615 620
 Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
 625 630 635 640
 Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
 645 650 655
 Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
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<211> 693

<212> PRT

<213> Homo sapiens

<400> 199

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Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
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Glu Cys Cys Phe Thr Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg Ile
 35           40           45

Met Asp Tyr Tyr Glu Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile Val
 50           55           60

Phe Ile Thr Lys Arg Gly His Ser Val Cys Thr Asn Pro Ser Asp Lys
 65           70           75           80

Trp Val Gln Asp Tyr Ile Lys Asp Met Lys Glu Asn Asp Ala His Lys
 85           90           95

Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Asp Ala His Lys
100           105           110

Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys
115           120           125

Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe
130           135           140

Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr
145           150           155           160

Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr
165           170           175

Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr
180           185           190

Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu
195           200           205

Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val
210           215           220

Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu
225           230           235           240

Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr
245           250           255

Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala
260           265           270

Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro
275           280           285

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Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln
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 Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys
 305 310 315 320
 Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe
 325 330 335
 Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu
 340 345 350
 Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu
 355 360 365
 Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys
 370 375 380
 Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu
 385 390 395 400
 Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp
 405 410 415
 Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp
 420 425 430
 Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp
 435 440 445
 Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr
 450 455 460
 Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys
 465 470 475 480
 Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile
 485 490 495
 Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln
 500 505 510
 Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr
 515 520 525
 Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys
 530 535 540
 Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr
 545 550 555 560
 Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro
 565 570 575
 Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg
 580 585 590

Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys
 595 600 605
 Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu
 610 615 620
 Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu
 625 630 635 640
 Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met
 645 650 655
 Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys
 660 665 670
 Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln
 675 680 685
 Ala Ala Leu Gly Leu
 690

<210> 200
 <211> 672
 <212> PRT
 <213> Homo sapiens

<400> 200
 Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15
 Ile Ser Ala His Ala Gly Pro Tyr His Pro Ser Glu Cys Cys Phe Thr
 20 25 30
 Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg Ile Met Asp Tyr Tyr Glu
 35 40 45
 Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile Val Phe Ile Thr Lys Arg
 50 55 60
 Gly His Ser Val Cys Thr Asn Pro Ser Asp Lys Trp Val Gln Asp Tyr
 65 70 75 80
 Ile Lys Asp Met Lys Glu Asn Asp Ala His Lys Ser Glu Val Ala His
 85 90 95
 Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile
 100 105 110
 Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
 115 120 125
 Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
 130 135 140
 Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys

145	150	155	160
Leu Cys Thr Val	Ala Thr Leu Arg Glu	Thr Tyr Gly Glu Met Ala Asp	
	165	170	175
Cys Cys Ala Lys	Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His		
	180	185	190
Lys Asp Asp Asn Pro Asn Leu	Pro Arg Leu Val Arg	Pro Glu Val Asp	
	195	200	205
Val Met Cys Thr Ala Phe His	Asp Asn Glu Glu Thr Phe Leu Lys Lys		
	210	215	220
Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu			
225	230	235	240
Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys			
	245	250	255
Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu			
	260	265	270
Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala			
	275	280	285
Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala			
	290	295	300
Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys			
305	310	315	320
Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp			
	325	330	335
Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys			
	340	345	350
Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys			
	355	360	365
Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu			
	370	375	380
Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys			
385	390	395	400
Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met			
	405	410	415
Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu			
	420	425	430
Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys			
	435	440	445
Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe			

450 455 460
 Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
 465 470 475 480
 Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
 485 490 495
 Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
 500 505 510
 Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
 515 520 525
 Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
 530 535 540
 Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
 545 550 555 560
 Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
 565 570 575
 Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
 580 585 590
 Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
 595 600 605
 Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
 610 615 620
 Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
 625 630 635 640
 Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
 645 650 655
 Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 660 665 670

<210> 201
 <211> 673
 <212> PRT
 <213> Homo sapiens

<400> 201
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30

Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Lys Val Leu Arg Arg His Ser Pro Lys Met Val Gln Gly Ser
 50 55 60
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 65 70 75 80
 Gly Cys Lys Val Leu Arg Arg His Asp Ala His Lys Ser Glu Val Ala
 85 90 95
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 100 105 110
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 115 120 125
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 130 135 140
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 145 150 155 160
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 165 170 175
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 180 185 190
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 195 200 205
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 210 215 220
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 225 230 235 240
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 245 250 255
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 260 265 270
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 275 280 285
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 290 295 300
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 305 310 315 320
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 325 330 335

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 340 345 350
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 355 360 365
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 370 375 380
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 385 390 395 400
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 405 410 415
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 420 425 430
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 435 440 445
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 450 455 460
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 465 470 475 480
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 485 490 495
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 500 505 510
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 515 520 525
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 530 535 540
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 545 550 555 560
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 565 570 575
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 580 585 590
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 595 600 605
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 610 615 620
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 625 630 635 640

Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
645 650 655

Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
660 665 670

Leu

<210> 202

<211> 850

<212> PRT

<213> Homo sapiens

<400> 202

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510

Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val
 610 615 620
 Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser
 625 630 635 640
 Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu
 645 650 655
 Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu
 660 665 670
 Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp
 675 680 685
 His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr
 690 695 700
 Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr
 705 710 715 720
 Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu
 725 730 735
 Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys
 740 745 750
 Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys
 755 760 765
 Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu
 770 775 780
 Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile
 785 790 795 800
 Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln
 805 810 815

Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu
820 825 830

Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu
835 840 845

Tyr Lys
850

<210> 203

<211> 767

<212> PRT

<213> Homo sapiens

<400> 203

Met Phe Lys Ser Val Val Tyr Ser Ile Leu Ala Ala Ser Leu Ala Asn
1 5 10 15

Ala Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly
20 25 30

Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu
35 40 45

Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr
50 55 60

Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp
65 70 75 80

Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr
85 90 95

Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu
100 105 110

Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn
115 120 125

Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe
130 135 140

His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala
145 150 155 160

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys
165 170 175

Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala
180 185 190

Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala
195 200 205

Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly

210	215	220
Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe 225 230 235 240		
Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr 245 250 255		
Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp 260 265 270		
Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile 275 280 285		
Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser 290 295 300		
His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro 305 310 315 320		
Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr 325 330 335		
Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala 340 345 350		
Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys 355 360 365		
Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His 370 375 380		
Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu 385 390 395 400		
Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly 405 410 415		
Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val 420 425 430		
Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly 435 440 445		
Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro 450 455 460		
Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu 465 470 475 480		
His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu 485 490 495		
Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu 500 505 510		
Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala		

515	520	525
Asp Ile Cys Thr Leu Ser	Glu Lys Glu Arg Gln	Ile Lys Lys Gln Thr
530	535	540
Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln		
545	550	555 560
Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys		
	565 570	575
Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu		
	580 585	590
Val Ala Ala Ser Gln Ala Ala Leu Gly Leu Cys Asp Leu Pro Gln Thr		
	595 600	605
His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg		
	610 615	620
Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe		
	625 630	635 640
Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro		
	645 650	655
Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys		
	660 665	670
Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr		
	675 680	685
Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly		
	690 695	700
Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala		
	705 710	715 720
Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys		
	725 730	735
Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser		
	740 745	750
Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu		
	755 760	765

<210> 204

<211> 769

<212> PRT

<213> Homo sapiens

<400> 204

Met	Leu	Leu	Gln	Ala	Phe	Leu	Phe	Leu	Leu	Ala	Gly	Phe	Ala	Ala	Lys
1						5					10				15

Ile Ser Ala Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
 20 25 30
 Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
 35 40 45
 Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
 50 55 60
 Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
 65 70 75 80
 Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
 85 90 95
 Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
 100 105 110
 Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
 115 120 125
 Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
 130 135 140
 Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu
 145 150 155 160
 Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe
 165 170 175
 Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp
 180 185 190
 Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly
 195 200 205
 Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys
 210 215 220
 Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
 225 230 235 240
 Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp
 245 250 255
 Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys
 260 265 270
 Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp
 275 280 285
 Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu
 290 295 300
 Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp
 305 310 315 320

Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys
 325 330 335
 Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu
 340 345 350
 Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu
 355 360 365
 Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp
 370 375 380
 Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val
 385 390 395 400
 Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
 405 410 415
 Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
 420 425 430
 Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
 435 440 445
 Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
 450 455 460
 Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
 465 470 475 480
 Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
 485 490 495
 Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
 500 505 510
 Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
 515 520 525
 His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
 530 535 540
 Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
 545 550 555 560
 Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
 565 570 575
 Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
 580 585 590
 Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu Cys Asp Leu Pro
 595 600 605
 Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln
 610 615 620

Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe
 625 630 635 640

Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr
 645 650 655

Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser
 660 665 670

Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe
 675 680 685

Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile
 690 695 700

Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile
 705 710 715 720

Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu
 725 730 735

Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met
 740 745 750

Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys
 755 760 765

Glu

<210> 205

<211> 779

<212> PRT

<213> Homo sapiens

<400> 205

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg Asp Ala His
 20 25 30

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
 35 40 45

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
 50 55 60

Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
 65 70 75 80

Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
 85 90 95

Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
 100 105 110
 Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
 115 120 125
 Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 130 135 140
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 145 150 155 160
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
 165 170 175
 Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 180 185 190
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 195 200 205
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 210 215 220
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 225 230 235 240
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 245 250 255
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 260 265 270
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 275 280 285
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 290 295 300
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 305 310 315 320
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 325 330 335
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 340 345 350
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 355 360 365
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 370 375 380
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 385 390 395 400

Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 405 410 415
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 420 425 430
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 435 440 445
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 450 455 460
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 465 470 475 480
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 485 490 495
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 500 505 510
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 515 520 525
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 530 535 540
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 545 550 555 560
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 565 570 575
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 580 585 590
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 595 600 605
 Gln Ala Ala Leu Gly Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly
 610 615 620
 Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu
 625 630 635 640
 Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu
 645 650 655
 Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu
 660 665 670
 Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala
 675 680 685
 Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln
 690 695 700

Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr
705 710 715 720

Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr
725 730 735

Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys
740 745 750

Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser
755 760 765

Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
770 775

<210> 206

<211> 674

<212> PRT

<213> Homo sapiens

<400> 206

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
35 40 45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg His Gly Glu Gly Thr
50 55 60

Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu
65 70 75 80

Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser Glu Val
85 90 95

Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
100 105 110

Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
115 120 125

Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
130 135 140

Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
145 150 155 160

Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
165 170 175

Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
180 185 190

Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
 195 200 205
 Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
 210 215 220
 Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
 225 230 235 240
 Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
 245 250 255
 Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
 260 265 270
 Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
 275 280 285
 Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 290 295 300
 Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
 305 310 315 320
 Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
 325 330 335
 Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
 340 345 350
 Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
 355 360 365
 Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
 370 375 380
 Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu
 385 390 395 400
 Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
 405 410 415
 Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val
 420 425 430
 Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys
 435 440 445
 Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp
 450 455 460
 Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn
 465 470 475 480
 Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu
 485 490 495

Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu
 500 505 510
 Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys
 515 520 525
 His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val
 530 535 540
 Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp
 545 550 555 560
 Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys
 565 570 575
 Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn
 580 585 590
 Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
 595 600 605
 Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His
 610 615 620
 Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
 625 630 635 640
 Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys
 645 650 655
 Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu
 660 665 670

Gly Leu

<210> 207
 <211> 634
 <212> PRT
 <213> Homo sapiens

<400> 207
 Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15
 Ile Ser Ala Ala Gly Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser
 20 25 30
 Cys Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly
 35 40 45
 Glu Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly
 50 55 60
 Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu
 65 70 75 80

Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr
 85 90 95
 Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp
 100 105 110
 Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr
 115 120 125
 Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu
 130 135 140
 Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn
 145 150 155 160
 Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe
 165 170 175
 His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala
 180 185 190
 Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys
 195 200 205
 Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala
 210 215 220
 Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala
 225 230 235 240
 Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly
 245 250 255
 Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe
 260 265 270
 Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr
 275 280 285
 Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp
 290 295 300
 Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile
 305 310 315 320
 Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser
 325 330 335
 His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro
 340 345 350
 Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr
 355 360 365
 Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala
 370 375 380

Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys
 385 390 395 400
 Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His
 405 410 415
 Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu
 420 425 430
 Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly
 435 440 445
 Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val
 450 455 460
 Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly
 465 470 475 480
 Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro
 485 490 495
 Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu
 500 505 510
 His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu
 515 520 525
 Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu
 530 535 540
 Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala
 545 550 555 560
 Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
 565 570 575
 Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln
 580 585 590
 Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys
 595 600 605
 Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu
 610 615 620
 Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 625 630

<210> 208

<211> 915

<212> PRT

<213> Homo sapiens

<400> 208

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30
 Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg His Gly Glu Gly Thr
 50 55 60
 Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu
 65 70 75 80
 Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser Glu Val
 85 90 95
 Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
 100 105 110
 Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
 115 120 125
 Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
 130 135 140
 Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
 145 150 155 160
 Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
 165 170 175
 Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
 180 185 190
 Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
 195 200 205
 Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
 210 215 220
 Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
 225 230 235 240
 Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
 245 250 255
 Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
 260 265 270
 Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
 275 280 285
 Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 290 295 300
 Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
 305 310 315 320

Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
 325 330 335
 Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
 340 345 350
 Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
 355 360 365
 Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
 370 375 380
 Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu
 385 390 395 400
 Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
 405 410 415
 Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val
 420 425 430
 Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys
 435 440 445
 Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp
 450 455 460
 Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn
 465 470 475 480
 Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu
 485 490 495
 Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu
 500 505 510
 Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys
 515 520 525
 His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val
 530 535 540
 Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp
 545 550 555 560
 Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys
 565 570 575
 Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn
 580 585 590
 Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
 595 600 605
 Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His
 610 615 620

Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
 625 630 635 640
 Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys
 645 650 655
 Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu
 660 665 670
 Gly Leu Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val
 675 680 685
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe
 690 695 700
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr
 705 710 715 720
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr
 725 730 735
 Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro
 740 745 750
 Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly
 755 760 765
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys
 770 775 780
 Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile
 785 790 795 800
 Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His
 805 810 815
 Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp
 820 825 830
 Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile
 835 840 845
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro
 850 855 860
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr
 865 870 875 880
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val
 885 890 895
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu
 900 905 910
 Leu Tyr Lys
 915

<210> 209

<211> 650

<212> PRT

<213> Homo sapiens

<400> 209

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60

Glu Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly
 65 70 75 80

Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu
 85 90 95

Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr
 100 105 110

Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp
 115 120 125

Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr
 130 135 140

Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu
 145 150 155 160

Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn
 165 170 175

Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe
 180 185 190

His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala
 195 200 205

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys
 210 215 220

Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala
 225 230 235 240

Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala
 245 250 255

Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly
 260 265 270
 Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe
 275 280 285
 Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr
 290 295 300
 Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp
 305 310 315 320
 Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile
 325 330 335
 Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser
 340 345 350
 His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro
 355 360 365
 Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr
 370 375 380
 Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala
 385 390 395 400
 Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys
 405 410 415
 Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His
 420 425 430
 Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu
 435 440 445
 Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly
 450 455 460
 Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val
 465 470 475 480
 Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly
 485 490 495
 Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro
 500 505 510
 Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu
 515 520 525
 His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu
 530 535 540
 Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu
 545 550 555 560

Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala
 565 570 575
 Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
 580 585 590
 Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln
 595 600 605
 Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys
 610 615 620
 Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu
 625 630 635 640
 Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 645 650

<210> 210
 <211> 658
 <212> PRT
 <213> Homo sapiens

<400> 210

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30
 Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Glu Val Ala His Arg Phe Lys Asp Leu Asp Ala His Lys Ser Glu Val
 65 70 75 80
 Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
 85 90 95
 Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
 100 105 110
 Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
 115 120 125
 Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
 130 135 140
 Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
 145 150 155 160
 Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu

165	170	175
Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu		
180	185	190
Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu		
195	200	205
Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala		
210	215	220
Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu		
225	230	235
Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp		
245	250	255
Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys		
260	265	270
Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala		
275	280	285
Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val		
290	295	300
Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His		
305	310	315
Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr		
325	330	335
Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys		
340	345	350
Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn		
355	360	365
Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu		
370	375	380
Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu		
385	390	395
Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val		
405	410	415
Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys		
420	425	430
Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp		
435	440	445
Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn		
450	455	460
Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu		

465					470					475					480
Leu	Val	Arg	Tyr	Thr	Lys	Lys	Val	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu
				485					490					495	
Val	Glu	Val	Ser	Arg	Asn	Leu	Gly	Lys	Val	Gly	Ser	Lys	Cys	Cys	Lys
			500					505					510		
His	Pro	Glu	Ala	Lys	Arg	Met	Pro	Cys	Ala	Glu	Asp	Tyr	Leu	Ser	Val
		515					520					525			
Val	Leu	Asn	Gln	Leu	Cys	Val	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Asp
	530					535					540				
Arg	Val	Thr	Lys	Cys	Cys	Thr	Glu	Ser	Leu	Val	Asn	Arg	Arg	Pro	Cys
545					550					555					560
Phe	Ser	Ala	Leu	Glu	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Asn
			565						570					575	
Ala	Glu	Thr	Phe	Thr	Phe	His	Ala	Asp	Ile	Cys	Thr	Leu	Ser	Glu	Lys
			580					585					590		
Glu	Arg	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Val	Glu	Leu	Val	Lys	His
		595				600						605			
Lys	Pro	Lys	Ala	Thr	Lys	Glu	Gln	Leu	Lys	Ala	Val	Met	Asp	Asp	Phe
	610					615					620				
Ala	Ala	Phe	Val	Glu	Lys	Cys	Cys	Lys	Ala	Asp	Asp	Lys	Glu	Thr	Cys
625					630					635					640
Phe	Ala	Glu	Glu	Gly	Lys	Lys	Leu	Val	Ala	Ala	Ser	Gln	Ala	Ala	Leu
				645					650					655	

Gly Leu

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<210> 211
<211> 641
<212> PRT
<213> Homo sapiens
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<400> 211
Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
  1                      5                      10                      15

Tyr Ser Arg Gly Val Phe Arg Arg Ser Pro Lys Met Val Gln Gly Ser
      20                      25                      30

Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
      35                      40                      45

Gly Cys Lys Val Leu Arg Arg His Asp Ala His Lys Ser Glu Val Ala
      50                      55                      60

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His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 65 70 75 80
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 85 90 95
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 100 105 110
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 115 120 125
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 130 135 140
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 145 150 155 160
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 165 170 175
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 180 185 190
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 195 200 205
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 210 215 220
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 225 230 235 240
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 245 250 255
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 260 265 270
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 275 280 285
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 290 295 300
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 305 310 315 320
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 325 330 335
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 340 345 350
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 355 360 365

Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 370 375 380
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 385 390 395 400
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 405 410 415
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 420 425 430
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 435 440 445
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 450 455 460
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 465 470 475 480
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 485 490 495
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 500 505 510
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 515 520 525
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 530 535 540
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 545 550 555 560
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 565 570 575
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 580 585 590
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 595 600 605
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 610 615 620
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 625 630 635 640
 Leu

<210> 212

<211> 647

<212> PRT

<213> Homo sapiens

<400> 212

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Asp Ala
 50 55 60

His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
 65 70 75 80

Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
 85 90 95

Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
 100 105 110

Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu
 115 120 125

His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
 130 135 140

Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
 145 150 155 160

Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
 165 170 175

Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
 180 185 190

Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
 195 200 205

Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
 210 215 220

Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
 225 230 235 240

Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
 245 250 255

Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
 260 265 270

Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala

275					280					285					
Glu	Phe	Ala	Glu	Val	Ser	Lys	Leu	Val	Thr	Asp	Leu	Thr	Lys	Val	His
290						295					300				
Thr	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala
305					310					315					320
Asp	Leu	Ala	Lys	Tyr	Ile	Cys	Glu	Asn	Gln	Asp	Ser	Ile	Ser	Ser	Lys
				325					330					335	
Leu	Lys	Glu	Cys	Cys	Glu	Lys	Pro	Leu	Leu	Glu	Lys	Ser	His	Cys	Ile
			340					345					350		
Ala	Glu	Val	Glu	Asn	Asp	Glu	Met	Pro	Ala	Asp	Leu	Pro	Ser	Leu	Ala
			355				360					365			
Ala	Asp	Phe	Val	Glu	Ser	Lys	Asp	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala
	370					375					380				
Lys	Asp	Val	Phe	Leu	Gly	Met	Phe	Leu	Tyr	Glu	Tyr	Ala	Arg	Arg	His
385					390					395					400
Pro	Asp	Tyr	Ser	Val	Val	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Thr	Tyr	Glu
				405					410					415	
Thr	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Ala	Ala	Asp	Pro	His	Glu	Cys	Tyr
			420					425					430		
Ala	Lys	Val	Phe	Asp	Glu	Phe	Lys	Pro	Leu	Val	Glu	Glu	Pro	Gln	Asn
			435				440					445			
Leu	Ile	Lys	Gln	Asn	Cys	Glu	Leu	Phe	Glu	Gln	Leu	Gly	Glu	Tyr	Lys
	450					455					460				
Phe	Gln	Asn	Ala	Leu	Leu	Val	Arg	Tyr	Thr	Lys	Lys	Val	Pro	Gln	Val
465					470					475				480	
Ser	Thr	Pro	Thr	Leu	Val	Glu	Val	Ser	Arg	Asn	Leu	Gly	Lys	Val	Gly
				485				490					495		
Ser	Lys	Cys	Cys	Lys	His	Pro	Glu	Ala	Lys	Arg	Met	Pro	Cys	Ala	Glu
			500				505					510			
Asp	Tyr	Leu	Ser	Val	Val	Leu	Asn	Gln	Leu	Cys	Val	Leu	His	Glu	Lys
			515				520					525			
Thr	Pro	Val	Ser	Asp	Arg	Val	Thr	Lys	Cys	Cys	Thr	Glu	Ser	Leu	Val
			530			535					540				
Asn	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Glu	Val	Asp	Glu	Thr	Tyr	Val
545					550					555				560	
Pro	Lys	Glu	Phe	Asn	Ala	Glu	Thr	Phe	Thr	Phe	His	Ala	Asp	Ile	Cys
				565				570					575		
Thr	Leu	Ser	Glu	Lys	Glu	Arg	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Val

580 585 590
 Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala
 595 600 605
 Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp
 610 615 620
 Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
 625 630 635 640
 Ser Gln Ala Ala Leu Gly Leu
 645

<210> 213
 <211> 649
 <212> PRT
 <213> Homo sapiens

<400> 213

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30
 Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
 65 70 75 80
 Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
 85 90 95
 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
 100 105 110
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
 115 120 125
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 130 135 140
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
 145 150 155 160
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 165 170 175
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 180 185 190

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 195 200 205
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
 210 215 220
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
 225 230 235 240
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
 245 250 255
 Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 260 265 270
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
 275 280 285
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
 290 295 300
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
 305 310 315 320
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
 325 330 335
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
 340 345 350
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
 355 360 365
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
 370 375 380
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
 385 390 395 400
 Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
 405 410 415
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
 420 425 430
 Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
 435 440 445
 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
 450 455 460
 Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
 465 470 475 480
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
 485 490 495

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
 500 505 510
 Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
 515 520 525
 Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
 530 535 540
 Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
 545 550 555 560
 Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
 565 570 575
 Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
 580 585 590
 Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
 595 600 605
 Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
 610 615 620
 Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
 625 630 635 640
 Ala Ala Ser Gln Ala Ala Leu Gly Leu
 645
 <210> 214
 <211> 648
 <212> PRT
 <213> Homo sapiens
 <400> 214
 Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30
 Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Asp
 50 55 60
 Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
 65 70 75 80
 Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
 85 90 95
 Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
 100 105 110

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
 115 120 125
 Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
 130 135 140
 Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
 145 150 155 160
 Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
 165 170 175
 Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
 180 185 190
 Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
 195 200 205
 His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
 210 215 220
 Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
 225 230 235 240
 Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
 245 250 255
 Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
 260 265 270
 Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
 275 280 285
 Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
 290 295 300
 His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
 305 310 315 320
 Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
 325 330 335
 Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
 340 345 350
 Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
 355 360 365
 Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
 370 375 380
 Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
 385 390 395 400
 His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
 405 410 415

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
 420 425 430
 Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
 435 440 445
 Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
 450 455 460
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 465 470 475 480
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 485 490 495
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 500 505 510
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 515 520 525
 Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 530 535 540
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 545 550 555 560
 Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
 565 570 575
 Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
 580 585 590
 Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
 595 600 605
 Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
 610 615 620
 Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
 625 630 635 640
 Ala Ser Gln Ala Ala Leu Gly Leu
 645

<210> 215

<211> 653

<212> PRT

<213> Homo sapiens

<400> 215

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Glu Val Ala His Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys
 65 70 75 80
 Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala
 85 90 95
 Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn
 100 105 110
 Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu
 115 120 125
 Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr
 130 135 140
 Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala
 145 150 155 160
 Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp
 165 170 175
 Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys
 180 185 190
 Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr
 195 200 205
 Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe
 210 215 220
 Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala
 225 230 235 240
 Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu
 245 250 255
 Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln
 260 265 270
 Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser
 275 280 285
 Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr
 290 295 300
 Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu
 305 310 315 320
 Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln
 325 330 335

Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu
 340 345 350
 Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala
 355 360 365
 Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys
 370 375 380
 Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr
 385 390 395 400
 Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg
 405 410 415
 Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala
 420 425 430
 Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu
 435 440 445
 Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu
 450 455 460
 Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr
 465 470 475 480
 Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg
 485 490 495
 Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys
 500 505 510
 Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu
 515 520 525
 Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys
 530 535 540
 Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu
 545 550 555 560
 Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr
 565 570 575
 Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys
 580 585 590
 Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr
 595 600 605
 Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu
 610 615 620
 Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
 625 630 635 640

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
645 650

<210> 216

<211> 657

<212> PRT

<213> Homo sapiens

<400> 216

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
1 5 10 15
Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
20 25 30
Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
35 40 45
Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
50 55 60
Glu Val Ala His Arg Phe Lys Asp Asp Ala His Lys Ser Glu Val Ala
65 70 75 80
His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
85 90 95
Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
100 105 110
Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
115 120 125
Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
130 135 140
Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
145 150 155 160
Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
165 170 175
His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
180 185 190
Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
195 200 205
Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
210 215 220
Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
225 230 235 240

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 245 250 255
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 260 265 270
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 275 280 285
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 290 295 300
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 305 310 315 320
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 325 330 335
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 340 345 350
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 355 360 365
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 370 375 380
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 385 390 395 400
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 405 410 415
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 420 425 430
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 435 440 445
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 450 455 460
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 465 470 475 480
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 485 490 495
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 500 505 510
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 515 520 525
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 530 535 540

Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 545 550 555 560
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 565 570 575
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 580 585 590
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 595 600 605
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 610 615 620
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 625 630 635 640
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 645 650 655

Leu

<210> 217
 <211> 673
 <212> PRT
 <213> Homo sapiens

<400> 217

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Gly Val Phe Arg Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Lys Val Leu Arg Arg His Ser Pro Lys Met Val Gln Gly Ser
 50 55 60
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 65 70 75 80
 Gly Cys Lys Val Leu Arg Arg His Asp Ala His Lys Ser Glu Val Ala
 85 90 95
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 100 105 110
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 115 120 125
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp

130	135	140
Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp		
145	150	155 160
Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala		
	165	170 175
Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln		
	180	185 190
His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val		
	195	200 205
Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys		
	210	215 220
Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro		
	225	230 235 240
Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys		
	245	250 255
Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu		
	260	265 270
Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys		
	275	280 285
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val		
	290	295 300
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser		
	305	310 315 320
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly		
	325	330 335
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile		
	340	345 350
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu		
	355	360 365
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp		
	370	375 380
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser		
	385	390 395 400
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly		
	405	410 415
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val		
	420	425 430
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys		

435 440 445
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 450 455 460
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 465 470 475 480
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 485 490 495
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 500 505 510
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 515 520 525
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 530 535 540
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 545 550 555 560
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 565 570 575
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 580 585 590
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 595 600 605
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 610 615 620
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 625 630 635 640
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 645 650 655
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 660 665 670
 Leu
 <210> 218
 <211> 652
 <212> PRT
 <213> Homo sapiens
 <400> 218
 Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Glu Val Ala Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
 65 70 75 80
 Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
 85 90 95
 Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
 100 105 110
 Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
 115 120 125
 Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
 130 135 140
 Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
 145 150 155 160
 Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
 165 170 175
 Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
 180 185 190
 Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu
 195 200 205
 Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe
 210 215 220
 Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp
 225 230 235 240
 Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly
 245 250 255
 Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys
 260 265 270
 Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
 275 280 285
 Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp
 290 295 300
 Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys
 305 310 315 320
 Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp
 325 330 335

Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu
 340 345 350
 Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp
 355 360 365
 Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys
 370 375 380
 Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu
 385 390 395 400
 Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu
 405 410 415
 Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Asp
 420 425 430
 Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val
 435 440 445
 Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
 450 455 460
 Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
 465 470 475 480
 Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
 485 490 495
 Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
 500 505 510
 Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
 515 520 525
 Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
 530 535 540
 Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
 545 550 555 560
 Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
 565 570 575
 His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
 580 585 590
 Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
 595 600 605
 Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
 610 615 620
 Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
 625 630 635 640

Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
645 650

<210> 219

<211> 654

<212> PRT

<213> Homo sapiens

<400> 219

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
35 40 45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
50 55 60

Glu Val Ala His Arg Asp Ala His Lys Ser Glu Val Ala His Arg Phe
65 70 75 80

Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe
85 90 95

Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val
100 105 110

Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
115 120 125

Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
130 135 140

Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys
145 150 155 160

Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
165 170 175

Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met
180 185 190

Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu
195 200 205

Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu
210 215 220

Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala
225 230 235 240

Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp

245										250										255													
Glu	Gly	Lys	Ala	Ser	Ser	Ala	Lys	Gln	Arg	Leu	Lys	Cys	Ala	Ser	Leu																		
			260					265						270																			
Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu																		
		275					280					285																					
Ser	Gln	Arg	Phe	Pro	Lys	Ala	Glu	Phe	Ala	Glu	Val	Ser	Lys	Leu	Val																		
		290				295					300																						
Thr	Asp	Leu	Thr	Lys	Val	His	Thr	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu																		
305					310					315					320																		
Glu	Cys	Ala	Asp	Asp	Arg	Ala	Asp	Leu	Ala	Lys	Tyr	Ile	Cys	Glu	Asn																		
				325				330						335																			
Gln	Asp	Ser	Ile	Ser	Ser	Lys	Leu	Lys	Glu	Cys	Cys	Glu	Lys	Pro	Leu																		
			340				345						350																				
Leu	Glu	Lys	Ser	His	Cys	Ile	Ala	Glu	Val	Glu	Asn	Asp	Glu	Met	Pro																		
		355				360					365																						
Ala	Asp	Leu	Pro	Ser	Leu	Ala	Ala	Asp	Phe	Val	Glu	Ser	Lys	Asp	Val																		
		370				375				380																							
Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Met	Phe	Leu																		
385					390				395					400																			
Tyr	Glu	Tyr	Ala	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Val	Leu	Leu	Leu																		
			405				410						415																				
Arg	Leu	Ala	Lys	Thr	Tyr	Glu	Thr	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Ala																		
		420					425						430																				
Ala	Asp	Pro	His	Glu	Cys	Tyr	Ala	Lys	Val	Phe	Asp	Glu	Phe	Lys	Pro																		
		435					440				445																						
Leu	Val	Glu	Glu	Pro	Gln	Asn	Leu	Ile	Lys	Gln	Asn	Cys	Glu	Leu	Phe																		
		450				455				460																							
Glu	Gln	Leu	Gly	Glu	Tyr	Lys	Phe	Gln	Asn	Ala	Leu	Leu	Val	Arg	Tyr																		
465					470				475					480																			
Thr	Lys	Lys	Val	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Val	Ser																		
			485					490					495																				
Arg	Asn	Leu	Gly	Lys	Val	Gly	Ser	Lys	Cys	Cys	Lys	His	Pro	Glu	Ala																		
		500					505					510																					
Lys	Arg	Met	Pro	Cys	Ala	Glu	Asp	Tyr	Leu	Ser	Val	Val	Leu	Asn	Gln																		
		515					520				525																						
Leu	Cys	Val	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Asp	Arg	Val	Thr	Lys																		
		530				535					540																						
Cys	Cys	Thr	Glu	Ser	Leu	Val	Asn	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu																		

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<210> 220
<211> 655
<212> PRT
<213> Homo sapiens
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<400> 220
Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
  1              5              10              15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
      20              25              30

Gly Thr Phe Thr Ser Asp Val Ser Tyr Leu Glu Gly Gln Ala Ala
      35              40              45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
      50              55              60

Glu Val Ala His Arg Phe Asp Ala His Lys Ser Glu Val Ala His Arg
      65              70              75              80

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
      85              90              95

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
      100              105              110

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
      115              120              125

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
      130              135              140

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
      145              150              155              160

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Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
 165 170 175
 Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
 180 185 190
 Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
 195 200 205
 Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
 210 215 220
 Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
 225 230 235 240
 Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
 245 250 255
 Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
 260 265 270
 Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
 275 280 285
 Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
 290 295 300
 Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
 305 310 315 320
 Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
 325 330 335
 Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
 340 345 350
 Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
 355 360 365
 Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
 370 375 380
 Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
 385 390 395 400
 Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
 405 410 415
 Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
 420 425 430
 Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
 435 440 445
 Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
 450 455 460

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
 465 470 475 480
 Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
 485 490 495
 Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
 500 505 510
 Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
 515 520 525
 Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
 530 535 540
 Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
 545 550 555 560
 Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
 565 570 575
 Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln
 580 585 590
 Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys
 595 600 605
 Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe
 610 615 620
 Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu
 625 630 635 640
 Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 645 650 655

<210> 221

<211> 659

<212> PRT

<213> Homo sapiens

<400> 221

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30
 Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Glu Val Ala His Arg Phe Lys Asp Leu Gly Asp Ala His Lys Ser Glu
 65 70 75 80

Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu
 85 90 95
 Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp
 100 105 110
 His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val
 115 120 125
 Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe
 130 135 140
 Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu
 145 150 155 160
 Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
 165 170 175
 Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro
 180 185 190
 Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe
 195 200 205
 Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr
 210 215 220
 Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr
 225 230 235 240
 Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu
 245 250 255
 Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu
 260 265 270
 Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
 275 280 285
 Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu
 290 295 300
 Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys
 305 310 315 320
 His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys
 325 330 335
 Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys
 340 345 350
 Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu
 355 360 365
 Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val
 370 375 380

Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
 385 390 395 400
 Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser
 405 410 415
 Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu
 420 425 430
 Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe
 435 440 445
 Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln
 450 455 460
 Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala
 465 470 475 480
 Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr
 485 490 495
 Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys
 500 505 510
 Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser
 515 520 525
 Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
 530 535 540
 Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
 545 550 555 560
 Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
 565 570 575
 Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
 580 585 590
 Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
 595 600 605
 His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp
 610 615 620
 Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
 625 630 635 640
 Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
 645 650 655
 Leu Gly Leu

<210> 222

<211> 637

<212> PRT

<213> Homo sapiens

<400> 222

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Ser Leu Arg Arg Ser Ser Cys Phe
 20 25 30

Gly Gly Arg Met Asp Arg Ile Gly Ala Gln Ser Gly Leu Gly Cys Asn
 35 40 45

Ser Phe Arg Tyr Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys
 50 55 60

Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala
 65 70 75 80

Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn
 85 90 95

Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu
 100 105 110

Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr
 115 120 125

Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala
 130 135 140

Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp
 145 150 155 160

Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys
 165 170 175

Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr
 180 185 190

Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe
 195 200 205

Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala
 210 215 220

Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu
 225 230 235 240

Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln
 245 250 255

Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser
 260 265 270

Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr
 275 280 285

Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu
 290 295 300
 Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln
 305 310 315 320
 Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu
 325 330 335
 Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala
 340 345 350
 Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys
 355 360 365
 Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr
 370 375 380
 Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg
 385 390 395 400
 Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala
 405 410 415
 Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu
 420 425 430
 Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu
 435 440 445
 Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr
 450 455 460
 Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg
 465 470 475 480
 Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys
 485 490 495
 Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu
 500 505 510
 Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys
 515 520 525
 Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu
 530 535 540
 Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr
 545 550 555 560
 Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys
 565 570 575
 Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr
 580 585 590

Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu
595 600 605

Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
610 615 620

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
625 630 635

<210> 223

<211> 646

<212> PRT

<213> Homo sapiens

<400> 223

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
35 40 45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala Asp Ala His
50 55 60

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
65 70 75 80

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
85 90 95

Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
100 105 110

Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
115 120 125

Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
130 135 140

Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
145 150 155 160

Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
165 170 175

Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
180 185 190

Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
195 200 205

Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 210 215 220
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 225 230 235 240
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 245 250 255
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 260 265 270
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 275 280 285
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 290 295 300
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 305 310 315 320
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 325 330 335
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 340 345 350
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 355 360 365
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 370 375 380
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 385 390 395 400
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 405 410 415
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 420 425 430
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 435 440 445
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 450 455 460
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 465 470 475 480
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 485 490 495
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 500 505 510

Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 515 520 525
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 530 535 540
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 545 550 555 560
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 565 570 575
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 580 585 590
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 595 600 605
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 610 615 620
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 625 630 635 640
 Gln Ala Ala Leu Gly Leu
 645

<210> 224
 <211> 651
 <212> PRT
 <213> Homo sapiens

<400> 224
 Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15
 Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30
 Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Glu Val Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu
 65 70 75 80
 Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr
 85 90 95
 Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val
 100 105 110
 Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys

115	120	125
Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala 130 135 140		
Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln 145 150 155 160		
Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro 165 170 175		
Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala 180 185 190		
Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile 195 200 205		
Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala 210 215 220		
Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys 225 230 235 240		
Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys 245 250 255		
Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe 260 265 270		
Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg 275 280 285		
Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu 290 295 300		
Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala 305 310 315 320		
Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser 325 330 335		
Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys 340 345 350		
Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu 355 360 365		
Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn 370 375 380		
Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr 385 390 395 400		
Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala 405 410 415		
Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro		

420 425 430
 His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu -
 435 440 445
 Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
 450 455 460
 Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
 465 470 475 480
 Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
 485 490 495
 Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
 500 505 510
 Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
 515 520 525
 Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
 530 535 540
 Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
 545 550 555 560
 Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
 565 570 575
 Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
 580 585 590
 Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
 595 600 605
 Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
 610 615 620
 Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
 625 630 635 640
 Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 645 650

<210> 225

<211> 656

<212> PRT

<213> Homo sapiens

<400> 225

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45
 Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60
 Glu Val Ala His Arg Phe Lys Asp Ala His Lys Ser Glu Val Ala His
 65 70 75 80
 Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile
 85 90 95
 Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
 100 105 110
 Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
 115 120 125
 Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
 130 135 140
 Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp
 145 150 155 160
 Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
 165 170 175
 Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp
 180 185 190
 Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys
 195 200 205
 Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
 210 215 220
 Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys
 225 230 235 240
 Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu
 245 250 255
 Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala
 260 265 270
 Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
 275 280 285
 Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys
 290 295 300
 Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp
 305 310 315 320
 Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys
 325 330 335

Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys
 340 345 350
 Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu
 355 360 365
 Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys
 370 375 380
 Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met
 385 390 395 400
 Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu
 405 410 415
 Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys
 420 425 430
 Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe
 435 440 445
 Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
 450 455 460
 Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
 465 470 475 480
 Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
 485 490 495
 Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
 500 505 510
 Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
 515 520 525
 Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
 530 535 540
 Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
 545 550 555 560
 Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
 565 570 575
 Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
 580 585 590
 Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
 595 600 605
 Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
 610 615 620
 Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
 625 630 635 640

Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 645 650 655

<210> 226

<211> 654

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (237)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 226

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15

Ile Ser Ala Ile Lys Pro Glu Ala Pro Gly Glu Asp Ala Ser Pro Glu
 20 25 30

Glu Leu Asn Arg Tyr Tyr Ala Ser Leu Arg His Tyr Leu Asn Leu Val
 35 40 45

Thr Arg Gln Arg Tyr Asp Ala His Lys Ser Glu Val Ala His Arg Phe
 50 55 60

Lys Asp Leu Gly Glu Asp Ala His Lys Ser Glu Val Ala His Arg Phe
 65 70 75 80

Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe
 85 90 95

Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val
 100 105 110

Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
 115 120 125

Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
 130 135 140

Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys
 145 150 155 160

Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
 165 170 175

Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met
 180 185 190

Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu

195	200	205
Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu		
210	215	220
Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Xaa Cys Gln Ala		
225	230	240
Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp		
	245	250 255
Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu		
	260	265 270
Gln Lys Ile Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu		
	275	280 285
Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val		
	290	295 300
Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu		
305	310	315 320
Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn		
	325	330 335
Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu		
	340	345 350
Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro		
	355	360 365
Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val		
	370	375 380
Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu		
385	390	395 400
Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu		
	405	410 415
Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala		
	420	425 430
Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro		
	435	440 445
Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe		
	450	455 460
Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr		
465	470	475 480
Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser		
	485	490 495
Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala		

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<210> 227
<211> 667
<212> PRT
<213> Homo sapiens
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<400> 227
Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
  1             5             10             15

Tyr Ser Arg Ser Leu Asp Lys Arg Ser Pro Lys Met Val Gln Gly Ser
      20             25             30

Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
      35             40             45

Gly Cys Lys Val Leu Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe
      50             55             60

Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys
  65             70             75             80

Val Leu Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu
      85             90             95

Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr
      100            105            110

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Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val
 115 120 125
 Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys
 130 135 140
 Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala
 145 150 155 160
 Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln
 165 170 175
 Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
 180 185 190
 Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala
 195 200 205
 Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile
 210 215 220
 Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala
 225 230 235 240
 Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys
 245 250 255
 Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys
 260 265 270
 Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe
 275 280 285
 Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg
 290 295 300
 Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu
 305 310 315 320
 Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
 325 330 335
 Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser
 340 345 350
 Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys
 355 360 365
 Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu
 370 375 380
 Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn
 385 390 395 400
 Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr
 405 410 415

Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala
 420 425 430
 Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro
 435 440 445
 His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu
 450 455 460
 Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
 465 470 475 480
 Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
 485 490 495
 Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
 500 505 510
 Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
 515 520 525
 Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
 530 535 540
 Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
 545 550 555 560
 Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
 565 570 575
 Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
 580 585 590
 Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
 595 600 605
 Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
 610 615 620
 Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
 625 630 635 640
 Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
 645 650 655
 Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 660 665

<210> 228

<211> 633

<212> PRT

<213> Homo sapiens

<400> 228

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15
 Ile Ser Ala Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg
 20 25 30
 Lys Met Asp Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys Val Leu
 35 40 45
 Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
 50 55 60
 Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
 65 70 75 80
 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
 85 90 95
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
 100 105 110
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 115 120 125
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
 130 135 140
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 145 150 155 160
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 165 170 175
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 180 185 190
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
 195 200 205
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
 210 215 220
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
 225 230 235 240
 Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 245 250 255
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
 260 265 270
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
 275 280 285
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
 290 295 300

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
 305 310 315 320
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
 325 330 335
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
 340 345 350
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
 355 360 365
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
 370 375 380
 Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
 385 390 395 400
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
 405 410 415
 Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
 420 425 430
 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
 435 440 445
 Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
 450 455 460
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
 465 470 475 480
 Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
 485 490 495
 Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
 500 505 510
 Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
 515 520 525
 Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
 530 535 540
 Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
 545 550 555 560
 Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
 565 570 575
 Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
 580 585 590
 Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
 595 600 605

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
610 615 620

Ala Ala Ser Gln Ala Ala Leu Gly Leu
625 630

<210> 229

<211> 638

<212> PRT

<213> Homo sapiens

<400> 229

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
1 5 10 15

Ile Ser Ala Ile Lys Pro Glu Ala Pro Gly Glu Asp Ala Ser Pro Glu
20 25 30

Glu Leu Asn Arg Tyr Tyr Ala Ser Leu Arg His Tyr Leu Asn Leu Val
35 40 45

Thr Arg Gln Arg Tyr Asp Ala His Lys Ser Glu Val Ala His Arg Phe
50 55 60

Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe
65 70 75 80

Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val
85 90 95

Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
100 105 110

Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
115 120 125

Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys
130 135 140

Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
145 150 155 160

Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met
165 170 175

Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu
180 185 190

Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu
195 200 205

Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala
210 215 220

Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp

225	230	235	240
Glu Gly Lys Ala Ser	Ser Ala Lys Gln Arg	Leu Lys Cys Ala Ser	Leu
245	250	255	
Gln Lys Phe Gly Glu Arg Ala Phe	Lys Ala Trp Ala Val Ala Arg	Leu	
260	265	270	
Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val	Ser Lys Leu Val		
275	280	285	
Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu			
290	295	300	
Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn			
305	310	315	320
Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu			
325	330	335	
Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro			
340	345	350	
Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val			
355	360	365	
Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu			
370	375	380	
Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu			
385	390	395	400
Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala			
405	410	415	
Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro			
420	425	430	
Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe			
435	440	445	
Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr			
450	455	460	
Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser			
465	470	475	480
Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala			
485	490	495	
Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln			
500	505	510	
Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys			
515	520	525	
Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu			

530 535 540
 Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe
 545 550 555 560
 Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile
 565 570 575
 Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala
 580 585 590
 Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val
 595 600 605
 Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu
 610 615 620
 Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 625 630 635

<210> 230
 <211> 641
 <212> PRT
 <213> Homo sapiens

<400> 230
 Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Gly Val Phe Arg Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Lys Val Leu Arg Arg His Asp Ala His Lys Ser Glu Val Ala
 50 55 60
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 65 70 75 80
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 85 90 95
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 100 105 110
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 115 120 125
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 130 135 140
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 145 150 155 160

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 165 170 175
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 180 185 190
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 195 200 205
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 210 215 220
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 225 230 235 240
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 245 250 255
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 260 265 270
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 275 280 285
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 290 295 300
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 305 310 315 320
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 325 330 335
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 340 345 350
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 355 360 365
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 370 375 380
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 385 390 395 400
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 405 410 415
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 420 425 430
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 435 440 445
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 450 455 460

Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 465 470 475 480
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 485 490 495
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 500 505 510
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 515 520 525
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 530 535 540
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 545 550 555 560
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 565 570 575
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 580 585 590
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 595 600 605
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 610 615 620
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 625 630 635 640
 Leu

<210> 231
 <211> 673
 <212> PRT
 <213> Homo sapiens

<400> 231
 Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Gly Val Phe Arg Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Lys Val Leu Arg Arg His Ser Pro Lys Met Val Gln Gly Ser
 50 55 60

Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 65 70 75 80
 Gly Cys Lys Val Leu Arg Arg His Asp Ala His Lys Ser Glu Val Ala
 85 90 95
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 100 105 110
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 115 120 125
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 130 135 140
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 145 150 155 160
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 165 170 175
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 180 185 190
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 195 200 205
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 210 215 220
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 225 230 235 240
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 245 250 255
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 260 265 270
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 275 280 285
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 290 295 300
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 305 310 315 320
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 325 330 335
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 340 345 350
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 355 360 365

Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 370 375 380
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 385 390 395 400
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 405 410 415
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 420 425 430
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 435 440 445
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 450 455 460
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 465 470 475 480
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 485 490 495
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 500 505 510
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 515 520 525
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 530 535 540
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 545 550 555 560
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 565 570 575
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 580 585 590
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 595 600 605
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 610 615 620
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 625 630 635 640
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Lys Glu Thr Cys Phe
 645 650 655
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 660 665 670

Leu

<210> 232

<211> 642

<212> PRT

<213> Homo sapiens

<400> 232

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser

143

545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ala Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp
 610 615 620
 Asn Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile
 625 630 635 640
 Thr Asp

<210> 233
 <211> 642
 <212> PRT
 <213> Homo sapiens

<400> 233
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg His Ala Asp Gly Ser Phe Ser Asp
 20 25 30
 Glu Met Asn Thr Ile Leu Asp Asn Leu Ala Ala Arg Asp Phe Ile Asn
 35 40 45
 Trp Leu Ile Gln Thr Lys Ile Thr Asp Asp Ala His Lys Ser Glu Val
 50 55 60
 Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
 65 70 75 80
 Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
 85 90 95
 Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
 100 105 110
 Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
 115 120 125
 Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
 130 135 140
 Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
 145 150 155 160

Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
 165 170 175
 Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
 180 185 190
 Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
 195 200 205
 Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
 210 215 220
 Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
 225 230 235 240
 Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
 245 250 255
 Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 260 265 270
 Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
 275 280 285
 Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
 290 295 300
 Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
 305 310 315 320
 Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
 325 330 335
 Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
 340 345 350
 Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu
 355 360 365
 Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
 370 375 380
 Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val
 385 390 395 400
 Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys
 405 410 415
 Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp
 420 425 430
 Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn
 435 440 445
 Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu
 450 455 460

Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu
 465 470 475 480
 Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys
 485 490 495
 His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val
 500 505 510
 Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp
 515 520 525
 Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys
 530 535 540
 Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn
 545 550 555 560
 Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
 565 570 575
 Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His
 580 585 590
 Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
 595 600 605
 Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys
 610 615 620
 Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu
 625 630 635 640
 Gly Leu

<210> 234

<211> 630

<212> PRT

<213> Homo sapiens

<400> 234

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15

Ile Ser Ala Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg
 20 25 30

Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Asp Ala His
 35 40 45

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
 50 55 60

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
 65 70 75 80
 Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
 85 90 95
 Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
 100 105 110
 Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
 115 120 125
 Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
 130 135 140
 Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 145 150 155 160
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 165 170 175
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
 180 185 190
 Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 195 200 205
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 210 215 220
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 225 230 235 240
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 245 250 255
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 260 265 270
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 275 280 285
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 290 295 300
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 305 310 315 320
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 325 330 335
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 340 345 350
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 355 360 365

Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 370 375 380
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 385 390 395 400
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 405 410 415
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 420 425 430
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 435 440 445
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 450 455 460
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 465 470 475 480
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 485 490 495
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 500 505 510
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 515 520 525
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 530 535 540
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 545 550 555 560
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 565 570 575
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 580 585 590
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 595 600 605
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 610 615 620
 Gln Ala Ala Leu Gly Leu
 625 630

<210> 235

<211> 631

<212> PRT

<213> Homo sapiens

<400> 235

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15

Ile Ser Ala Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg
 20 25 30

Lys Met Asp Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys Asp Ala
 35 40 45

His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
 50 55 60

Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
 65 70 75 80

Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
 85 90 95

Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu
 100 105 110

His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
 115 120 125

Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
 130 135 140

Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
 145 150 155 160

Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
 165 170 175

Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
 180 185 190

Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
 195 200 205

Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
 210 215 220

Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
 225 230 235 240

Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
 245 250 255

Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala
 260 265 270

Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His
 275 280 285

Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala

290	295	300
Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys 305 310 315 320		
Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile 325 330 335		
Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala 340 345 350		
Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala 355 360 365		
Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His 370 375 380		
Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu 385 390 395 400		
Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr 405 410 415		
Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn 420 425 430		
Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys 435 440 445		
Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val 450 455 460		
Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly 465 470 475 480		
Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu 485 490 495		
Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys 500 505 510		
Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val 515 520 525		
Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val 530 535 540		
Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys 545 550 555 560		
Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val 565 570 575		
Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala 580 585 590		
Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp		

595 600 605
 Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
 610 615 620
 Ser Gln Ala Ala Leu Gly Leu
 625 630

 <210> 236
 <211> 632
 <212> PRT
 <213> Homo sapiens

 <400> 236
 Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15
 Ile Ser Ala Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg
 20 25 30
 Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Asp
 35 40 45
 Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
 50 55 60
 Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
 65 70 75 80
 Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
 85 90 95
 Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
 100 105 110
 Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
 115 120 125
 Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
 130 135 140
 Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
 145 150 155 160
 Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
 165 170 175
 Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
 180 185 190
 His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
 195 200 205
 Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
 210 215 220

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
 225 230 235 240
 Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
 245 250 255
 Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
 260 265 270
 Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
 275 280 285
 His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
 290 295 300
 Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
 305 310 315 320
 Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
 325 330 335
 Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
 340 345 350
 Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
 355 360 365
 Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
 370 375 380
 His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
 385 390 395 400
 Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
 405 410 415
 Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
 420 425 430
 Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
 435 440 445
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 450 455 460
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 465 470 475 480
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 485 490 495
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 500 505 510
 Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 515 520 525

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 530 535 540

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
 545 550 555 560

Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
 565 570 575

Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
 580 585 590

Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
 595 600 605

Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
 610 615 620

Ala Ser Gln Ala Ala Leu Gly Leu
 625 630

<210> 237
 <211> 642
 <212> PRT
 <213> Homo sapiens

<400> 237
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445

Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Gly Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp
 610 615 620
 Asn Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile
 625 630 635 640
 Thr Asp

<210> 238

<211> 642

<212> PRT

<213> Homo sapiens

<400> 238

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg His Gly Asp Gly Ser Phe Ser Asp
 20 25 30
 Glu Met Asn Thr Ile Leu Asp Asn Leu Ala Ala Arg Asp Phe Ile Asn
 35 40 45
 Trp Leu Ile Gln Thr Lys Ile Thr Asp Asp Ala His Lys Ser Glu Val

50 55 60
 Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
 65 70 75 80
 Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
 85 90 95
 Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
 100 105 110
 Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
 115 120 125
 Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
 130 135 140
 Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
 145 150 155 160
 Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
 165 170 175
 Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
 180 185 190
 Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
 195 200 205
 Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
 210 215 220
 Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
 225 230 235 240
 Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
 245 250 255
 Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 260 265 270
 Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
 275 280 285
 Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
 290 295 300
 Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
 305 310 315 320
 Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
 325 330 335
 Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
 340 345 350
 Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu

355	360	365
Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu		
370	375	380
Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val		
385	390	395
Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys		
405	410	415
Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp		
420	425	430
Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn		
435	440	445
Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu		
450	455	460
Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu		
465	470	475
Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys		
485	490	495
His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val		
500	505	510
Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp		
515	520	525
Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys		
530	535	540
Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn		
545	550	555
Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys		
565	570	575
Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His		
580	585	590
Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe		
595	600	605
Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys		
610	615	620
Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu		
625	630	635
640		
Gly Leu		

<210> 239

<211> 636

<212> PRT

<213> Homo sapiens

<400> 239

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255

Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575

Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
580 585 590

Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
595 600 605

Leu His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys
610 615 620

Gln Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu
625 630 635

<210> 240

<211> 636

<212> PRT

<213> Homo sapiens

<400> 240

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Gly Ile Phe Thr Asp
20 25 30

Ser Tyr Ser Arg Tyr Arg Lys Gln Met Ala Val Lys Lys Tyr Leu Ala
35 40 45

Ala Val Leu Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
50 55 60

Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
65 70 75 80

Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
85 90 95

Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
100 105 110

Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
115 120 125

Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
130 135 140

Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
145 150 155 160

Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
165 170 175

Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu
180 185 190

Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe
 195 200 205
 Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp
 210 215 220
 Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly
 225 230 235 240
 Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys
 245 250 255
 Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
 260 265 270
 Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp
 275 280 285
 Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys
 290 295 300
 Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp
 305 310 315 320
 Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu
 325 330 335
 Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp
 340 345 350
 Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys
 355 360 365
 Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu
 370 375 380
 Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu
 385 390 395 400
 Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp
 405 410 415
 Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val
 420 425 430
 Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
 435 440 445
 Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
 450 455 460
 Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
 465 470 475 480
 Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
 485 490 495

Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
500 505 510

Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
515 520 525

Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
530 535 540

Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
545 550 555 560

His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
565 570 575

Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
580 585 590

Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
595 600 605

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
610 615 620

Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
625 630 635

<210> 241

<211> 647

<212> PRT

<213> Homo sapiens

<400> 241

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln

115					120					125					
His	Lys	Asp	Asp	Asn	Pro	Asn	Leu	Pro	Arg	Leu	Val	Arg	Pro	Glu	Val
130						135					140				
Asp	Val	Met	Cys	Thr	Ala	Phe	His	Asp	Asn	Glu	Glu	Thr	Phe	Leu	Lys
145					150					155					160
Lys	Tyr	Leu	Tyr	Glu	Ile	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro
				165					170					175	
Glu	Leu	Leu	Phe	Phe	Ala	Lys	Arg	Tyr	Lys	Ala	Ala	Phe	Thr	Glu	Cys
			180					185					190		
Cys	Gln	Ala	Ala	Asp	Lys	Ala	Ala	Cys	Leu	Leu	Pro	Lys	Leu	Asp	Glu
		195					200					205			
Leu	Arg	Asp	Glu	Gly	Lys	Ala	Ser	Ser	Ala	Lys	Gln	Arg	Leu	Lys	Cys
	210					215					220				
Ala	Ser	Leu	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val
225					230					235					240
Ala	Arg	Leu	Ser	Gln	Arg	Phe	Pro	Lys	Ala	Glu	Phe	Ala	Glu	Val	Ser
				245					250					255	
Lys	Leu	Val	Thr	Asp	Leu	Thr	Lys	Val	His	Thr	Glu	Cys	Cys	His	Gly
			260					265						270	
Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Asp	Leu	Ala	Lys	Tyr	Ile
	275						280					285			
Cys	Glu	Asn	Gln	Asp	Ser	Ile	Ser	Ser	Lys	Leu	Lys	Glu	Cys	Cys	Glu
	290					295					300				
Lys	Pro	Leu	Leu	Glu	Lys	Ser	His	Cys	Ile	Ala	Glu	Val	Glu	Asn	Asp
305					310					315					320
Glu	Met	Pro	Ala	Asp	Leu	Pro	Ser	Leu	Ala	Ala	Asp	Phe	Val	Glu	Ser
				325					330					335	
Lys	Asp	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly
			340					345						350	
Met	Phe	Leu	Tyr	Glu	Tyr	Ala	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Val
	355						360					365			
Leu	Leu	Leu	Arg	Leu	Ala	Lys	Thr	Tyr	Glu	Thr	Thr	Leu	Glu	Lys	Cys
	370					375						380			
Cys	Ala	Ala	Ala	Asp	Pro	His	Glu	Cys	Tyr	Ala	Lys	Val	Phe	Asp	Glu
385					390					395					400
Phe	Lys	Pro	Leu	Val	Glu	Glu	Pro	Gln	Asn	Leu	Ile	Lys	Gln	Asn	Cys
				405					410					415	
Glu	Leu	Phe	Glu	Gln	Leu	Gly	Glu	Tyr	Lys	Phe	Gln	Asn	Ala	Leu	Leu

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<210> 242
<211> 647
<212> PRT
<213> Homo sapiens
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<400> 242
Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1             5             10             15
Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Gly Ile Phe Thr Asp
          20             25             30

```

Ser Tyr Ser Arg Tyr Arg Lys Gln Met Ala Val Lys Lys Tyr Leu Ala
 35 40 45
 Ala Val Leu Gly Lys Arg Tyr Lys Gln Arg Val Lys Asn Lys Asp Ala
 50 55 60
 His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
 65 70 75 80
 Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
 85 90 95
 Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
 100 105 110
 Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu
 115 120 125
 His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
 130 135 140
 Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
 145 150 155 160
 Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
 165 170 175
 Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
 180 185 190
 Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
 195 200 205
 Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
 210 215 220
 Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
 225 230 235 240
 Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
 245 250 255
 Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
 260 265 270
 Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala
 275 280 285
 Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His
 290 295 300
 Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
 305 310 315 320
 Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys
 325 330 335

Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile
 340 345 350
 Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala
 355 360 365
 Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala
 370 375 380
 Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His
 385 390 395 400
 Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu
 405 410 415
 Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr
 420 425 430
 Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn
 435 440 445
 Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys
 450 455 460
 Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val
 465 470 475 480
 Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly
 485 490 495
 Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu
 500 505 510
 Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys
 515 520 525
 Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val
 530 535 540
 Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val
 545 550 555 560
 Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys
 565 570 575
 Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val
 580 585 590
 Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala
 595 600 605
 Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp
 610 615 620
 Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
 625 630 635 640

Ser Gln Ala Ala Leu Gly Leu
645

<210> 243

<211> 728

<212> PRT

<213> Homo sapiens

<400> 243

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
210 215 220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
225 230 235 240

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540

Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser
 610 615 620
 Ile Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met
 625 630 635 640
 Ser Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly
 645 650 655
 Gln Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr
 660 665 670
 Thr Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln
 675 680 685
 Cys Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys
 690 695 700
 Lys Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys
 705 710 715 720
 Thr Leu Thr Ile Lys Arg Gly Arg
 725

<210> 244

<211> 728

<212> PRT

<213> Homo sapiens

<400> 244

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Pro Ala Arg Arg Gly
 20 25 30
 Glu Leu Ser Val Cys Asp Ser Ile Ser Glu Trp Val Thr Ala Ala Asp
 35 40 45
 Lys Lys Thr Ala Val Asp Met Ser Gly Gly Thr Val Thr Val Leu Glu
 50 55 60
 Lys Val Pro Val Ser Lys Gly Gln Leu Lys Gln Tyr Phe Tyr Glu Thr

65		70		75		80
Lys Cys Asn Pro Met Gly Tyr Thr Lys Glu Gly Cys Arg Gly Ile Asp						
		85		90		95
Lys Arg His Trp Asn Ser Gln Cys Arg Thr Thr Gln Ser Tyr Val Arg						
		100		105		110
Ala Leu Thr Met Asp Ser Lys Lys Arg Ile Gly Trp Arg Phe Ile Arg						
		115		120		125
Ile Asp Thr Ser Cys Val Cys Thr Leu Thr Ile Lys Arg Gly Arg Asp						
		130		135		140
Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu						
		145		150		155
Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln						
		165		170		175
Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe						
		180		185		190
Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser						
		195		200		205
Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg						
		210		215		220
Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu						
		225		230		235
Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro						
		245		250		255
Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp						
		260		265		270
Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg						
		275		280		285
His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr						
		290		295		300
Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys						
		305		310		315
Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser						
		325		330		335
Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg						
		340		345		350
Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys						
		355		360		365
Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val						

370 375 380
 His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
 385 390 395 400
 Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
 405 410 415
 Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
 420 425 430
 Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
 435 440 445
 Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
 450 455 460
 Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
 465 470 475 480
 His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
 485 490 495
 Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
 500 505 510
 Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
 515 520 525
 Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
 530 535 540
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 545 550 555 560
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 565 570 575
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 580 585 590
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 595 600 605
 Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 610 615 620
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 625 630 635 640
 Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
 645 650 655
 Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
 660 665 670
 Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys

675 680 685
 Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
 690 695 700
 Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
 705 710 715 720
 Ala Ser Gln Ala Ala Leu Gly Leu
 725

<210> 245
 <211> 728
 <212> PRT
 <213> Homo sapiens

<400> 245
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510

Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser
 610 615 620
 Ile Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met
 625 630 635 640
 Ser Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly
 645 650 655
 Gln Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr
 660 665 670
 Thr Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln
 675 680 685
 Cys Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys
 690 695 700
 Lys Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys
 705 710 715 720
 Thr Leu Thr Ile Lys Arg Gly Arg
 725

<210> 246

<211> 728

<212> PRT

<213> Homo sapiens

<400> 246

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Pro Ala Arg Arg Gly
 20 25 30

Glu Leu Ser Val Cys Asp Ser Ile Ser Glu Trp Val Thr Ala Ala Asp
 35 40 45
 Lys Lys Thr Ala Val Asp Met Ser Gly Gly Thr Val Thr Val Leu Glu
 50 55 60
 Lys Val Pro Val Ser Lys Gly Gln Leu Lys Gln Tyr Phe Tyr Glu Thr
 65 70 75 80
 Lys Cys Asn Pro Met Gly Tyr Thr Lys Glu Gly Cys Arg Gly Ile Asp
 85 90 95
 Lys Arg His Trp Asn Ser Gln Cys Arg Thr Thr Gln Ser Tyr Val Arg
 100 105 110
 Ala Leu Thr Met Asp Ser Lys Lys Arg Ile Gly Trp Arg Phe Ile Arg
 115 120 125
 Ile Asp Thr Ser Cys Val Cys Thr Leu Thr Ile Lys Arg Gly Arg Asp
 130 135 140
 Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
 145 150 155 160
 Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
 165 170 175
 Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
 180 185 190
 Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
 195 200 205
 Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
 210 215 220
 Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
 225 230 235 240
 Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
 245 250 255
 Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
 260 265 270
 Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
 275 280 285
 His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
 290 295 300
 Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
 305 310 315 320
 Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
 325 330 335

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
 340 345 350
 Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
 355 360 365
 Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
 370 375 380
 His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
 385 390 395 400
 Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
 405 410 415
 Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
 420 425 430
 Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
 435 440 445
 Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
 450 455 460
 Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
 465 470 475 480
 His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
 485 490 495
 Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
 500 505 510
 Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
 515 520 525
 Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
 530 535 540
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 545 550 555 560
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 565 570 575
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 580 585 590
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 595 600 605
 Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 610 615 620
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 625 630 635 640

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
645 650 655

Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
660 665 670

Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
675 680 685

Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
690 695 700

Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
705 710 715 720

Ala Ser Gln Ala Ala Leu Gly Leu
725

<210> 247

<211> 728

<212> PRT

<213> Homo sapiens

<400> 247

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480

Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser
 610 615 620
 Ile Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met
 625 630 635 640
 Ser Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly
 645 650 655
 Gln Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr
 660 665 670
 Thr Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln
 675 680 685
 Cys Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys
 690 695 700
 Lys Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys
 705 710 715 720
 Thr Leu Thr Ile Lys Arg Gly Arg
 725

<210> 248

<211> 728

<212> PRT

<213> Homo sapiens

<400> 248

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Pro Ala Arg Arg Gly
 20 25 30
 Glu Leu Ser Val Cys Asp Ser Ile Ser Glu Trp Val Thr Ala Ala Asp
 35 40 45
 Lys Lys Thr Ala Val Asp Met Ser Gly Gly Thr Val Thr Val Leu Glu
 50 55 60
 Lys Val Pro Val Ser Lys Gly Gln Leu Lys Gln Tyr Phe Tyr Glu Thr
 65 70 75 80
 Lys Cys Asn Pro Met Gly Tyr Thr Lys Glu Gly Cys Arg Gly Ile Asp
 85 90 95
 Lys Arg His Trp Asn Ser Gln Cys Arg Thr Thr Gln Ser Tyr Val Arg
 100 105 110
 Ala Leu Thr Met Asp Ser Lys Lys Arg Ile Gly Trp Arg Phe Ile Arg
 115 120 125
 Ile Asp Thr Ser Cys Val Cys Thr Leu Thr Ile Lys Arg Gly Arg Asp
 130 135 140
 Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
 145 150 155 160
 Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
 165 170 175
 Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
 180 185 190
 Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
 195 200 205
 Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
 210 215 220
 Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
 225 230 235 240
 Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
 245 250 255
 Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
 260 265 270
 Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
 275 280 285
 His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
 290 295 300

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
 305 310 315 320
 Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
 325 330 335
 Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
 340 345 350
 Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
 355 360 365
 Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
 370 375 380
 His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
 385 390 395 400
 Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
 405 410 415
 Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
 420 425 430
 Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
 435 440 445
 Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
 450 455 460
 Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
 465 470 475 480
 His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
 485 490 495
 Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
 500 505 510
 Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
 515 520 525
 Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
 530 535 540
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 545 550 555 560
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 565 570 575
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 580 585 590
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 595 600 605

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 610 615 620
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 625 630 635 640
 Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
 645 650 655
 Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
 660 665 670
 Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
 675 680 685
 Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
 690 695 700
 Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
 705 710 715 720
 Ala Ser Gln Ala Ala Leu Gly Leu
 725

<210> 249
 <211> 801
 <212> PRT
 <213> Homo sapiens

<400> 249
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val

130	135	140
Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys		
145	150	155 160
Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro		
	165	170 175
Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys		
	180	185 190
Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu		
	195	200 205
Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys		
	210	215 220
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val		
	225	230 235 240
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser		
	245	250 255
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly		
	260	265 270
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile		
	275	280 285
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu		
	290	295 300
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp		
	305	310 315 320
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser		
	325	330 335
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly		
	340	345 350
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val		
	355	360 365
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys		
	370	375 380
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu		
	385	390 395 400
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys		
	405	410 415
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu		
	420	425 430
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val		

435	440	445
Glu Val Ser Arg Asn Leu	Gly Lys Val Gly Ser	Lys Cys Cys Lys His
450	455	460
Pro Glu Ala Lys Arg Met	Pro Cys Ala Glu Asp Tyr	Leu Ser Val Val
465	470	475
Leu Asn Gln Leu Cys Val	Leu His Glu Lys Thr	Pro Val Ser Asp Arg
485	490	495
Val Thr Lys Cys Cys Thr	Glu Ser Leu Val Asn Arg	Arg Pro Cys Phe
500	505	510
Ser Ala Leu Glu Val Asp	Glu Thr Tyr Val Pro	Lys Glu Phe Asn Ala
515	520	525
Glu Thr Phe Thr Phe His	Ala Asp Ile Cys Thr	Leu Ser Glu Lys Glu
530	535	540
Arg Gln Ile Lys Lys Gln	Thr Ala Leu Val Glu	Leu Val Lys His Lys
545	550	555
Pro Lys Ala Thr Lys Glu	Gln Leu Lys Ala Val	Met Asp Asp Phe Ala
565	570	575
Ala Phe Val Glu Lys Cys	Cys Lys Ala Asp Asp	Lys Glu Thr Cys Phe
580	585	590
Ala Glu Glu Gly Lys Lys	Leu Val Ala Ala Ser	Gln Ala Ala Leu Gly
595	600	605
Leu Phe Pro Leu Pro Ala	Gly Lys Arg Pro Pro	Glu Ala Pro Ala Glu
610	615	620
Asp Arg Ser Leu Gly Arg	Arg Arg Ala Pro Phe	Ala Leu Ser Ser Asp
625	630	635
Ser Asn Met Pro Glu Asp	Tyr Pro Asp Gln Phe	Asp Asp Val Met Asp
645	650	655
Phe Ile Gln Ala Thr Ile	Lys Arg Leu Lys Arg	Ser Pro Asp Lys Gln
660	665	670
Met Ala Val Leu Pro Arg	Arg Glu Arg Asn Arg	Gln Ala Ala Ala Ala
675	680	685
Asn Pro Glu Asn Ser Arg	Gly Lys Gly Arg Arg	Gly Gln Arg Gly Lys
690	695	700
Asn Arg Gly Cys Val Leu	Thr Ala Ile His Leu	Asn Val Thr Asp Leu
705	710	715
Gly Leu Gly Tyr Glu Thr	Lys Glu Glu Leu Ile	Phe Arg Tyr Cys Ser
725	730	735
Gly Ser Cys Asp Ala Ala	Glu Thr Thr Tyr Asp	Lys Ile Leu Lys Asn

740 745 750
 Leu Ser Arg Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln Ala Cys
 755 760 765
 Cys Arg Pro Ile Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn
 770 775 780
 Leu Val Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys
 785 790 795 800
 Ile

 <210> 250
 <211> 801
 <212> PRT
 <213> Homo sapiens

 <400> 250
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Phe Pro Leu Pro Ala Gly Lys Arg
 20 25 30
 Pro Pro Glu Ala Pro Ala Glu Asp Arg Ser Leu Gly Arg Arg Arg Ala
 35 40 45
 Pro Phe Ala Leu Ser Ser Asp Ser Asn Met Pro Glu Asp Tyr Pro Asp
 50 55 60
 Gln Phe Asp Asp Val Met Asp Phe Ile Gln Ala Thr Ile Lys Arg Leu
 65 70 75 80
 Lys Arg Ser Pro Asp Lys Gln Met Ala Val Leu Pro Arg Arg Glu Arg
 85 90 95
 Asn Arg Gln Ala Ala Ala Ala Asn Pro Glu Asn Ser Arg Gly Lys Gly
 100 105 110
 Arg Arg Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile
 115 120 125
 His Leu Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu
 130 135 140
 Leu Ile Phe Arg Tyr Cys Ser Gly Ser Cys Asp Ala Ala Glu Thr Thr
 145 150 155 160
 Tyr Asp Lys Ile Leu Lys Asn Leu Ser Arg Asn Arg Arg Leu Val Ser
 165 170 175
 Asp Lys Val Gly Gln Ala Cys Cys Arg Pro Ile Ala Phe Asp Asp Asp
 180 185 190

Leu Ser Phe Leu Asp Asp Asn Leu Val Tyr His Ile Leu Arg Lys His
 195 200 205
 Ser Ala Lys Arg Cys Gly Cys Ile Asp Ala His Lys Ser Glu Val Ala
 210 215 220
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 225 230 235 240
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 245 250 255
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 260 265 270
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 275 280 285
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 290 295 300
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 305 310 315 320
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 325 330 335
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 340 345 350
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 355 360 365
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 370 375 380
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 385 390 395 400
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 405 410 415
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 420 425 430
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 435 440 445
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 450 455 460
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 465 470 475 480
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 485 490 495

Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 500 505 510
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 515 520 525
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 530 535 540
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 545 550 555 560
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 565 570 575
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 580 585 590
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 595 600 605
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 610 615 620
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 625 630 635 640
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 645 650 655
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 660 665 670
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 675 680 685
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 690 695 700
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 705 710 715 720
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 725 730 735
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 740 745 750
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 755 760 765
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 770 775 780
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 785 790 795 800

Leu

<210> 251

<211> 787

<212> PRT

<213> Homo sapiens

<400> 251

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540

Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ile Trp Met Cys Arg Glu Gly Leu Leu Leu Ser His Arg Leu Gly
 610 615 620
 Pro Ala Leu Val Pro Leu His Arg Leu Pro Arg Thr Leu Asp Ala Arg
 625 630 635 640
 Ile Ala Arg Leu Ala Gln Tyr Arg Ala Leu Leu Gln Gly Ala Pro Asp
 645 650 655
 Ala Met Glu Leu Arg Glu Leu Thr Pro Trp Ala Gly Arg Pro Pro Gly
 660 665 670
 Pro Arg Arg Arg Ala Gly Pro Arg Arg Arg Arg Ala Arg Ala Arg Leu
 675 680 685
 Gly Ala Arg Pro Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu
 690 695 700
 Leu Gly Leu Gly Tyr Ala Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys
 705 710 715 720
 Ala Gly Ala Cys Glu Ala Ala Ala Arg Val Tyr Asp Leu Gly Leu Arg
 725 730 735
 Arg Leu Arg Gln Arg Arg Arg Leu Arg Arg Glu Arg Val Arg Ala Gln
 740 745 750
 Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp
 755 760 765
 Ala His Ser Arg Tyr His Thr Val His Glu Leu Ser Ala Arg Glu Cys
 770 775 780
 Ala Cys Val
 785

<210> 252

<211> 711

<212> PRT

<213> Homo sapiens

<400> 252

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala

1	5	10	15
Tyr Ser Arg Ser Leu Asp Lys Arg Ala Arg Leu Gly Ala Arg Pro Cys	20	25	30
Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr	35	40	45
Ala Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu	50	55	60
Ala Ala Ala Arg Val Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln Arg	65	70	75
Arg Arg Leu Arg Arg Glu Arg Val Arg Ala Gln Pro Cys Cys Arg Pro	85	90	95
Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Ala His Ser Arg Tyr	100	105	110
His Thr Val His Glu Leu Ser Ala Arg Glu Cys Ala Cys Val Asp Ala	115	120	125
His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn	130	135	140
Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys	145	150	155
Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala	165	170	175
Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu	180	185	190
His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu	195	200	205
Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg	210	215	220
Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg	225	230	235
Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn	245	250	255
Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His	260	265	270
Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys	275	280	285
Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu	290	295	300
Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala			

305		310		315		320
Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala						
	325			330		335
Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala						
	340		345			350
Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His						
	355		360			365
Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala						
	370		375			380
Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys						
	385		390		395	400
Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile						
		405		410		415
Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala						
		420		425		430
Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala						
	435		440			445
Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His						
	450		455			460
Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu						
	465		470		475	480
Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr						
		485		490		495
Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn						
	500		505			510
Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys						
	515		520			525
Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val						
	530		535			540
Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly						
	545		550		555	560
Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu						
		565		570		575
Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys						
	580		585			590
Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val						
	595		600			605
Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val						

610 615 620
 Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys
 625 630 635 640
 Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val
 645 650 655
 Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala
 660 665 670
 Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp
 675 680 685
 Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
 690 695 700
 Ser Gln Ala Ala Leu Gly Leu
 705 710
 <210> 253
 <211> 728
 <212> PRT
 <213> Homo sapiens
 <400> 253
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro

165										170										175									
Glu	Leu	Leu	Phe	Phe	Ala	Lys	Arg	Tyr	Lys	Ala	Ala	Phe	Thr	Glu	Cys														
			180					185						190															
Cys	Gln	Ala	Ala	Asp	Lys	Ala	Ala	Cys	Leu	Leu	Pro	Lys	Leu	Asp	Glu														
		195					200						205																
Leu	Arg	Asp	Glu	Gly	Lys	Ala	Ser	Ser	Ala	Lys	Gln	Arg	Leu	Lys	Cys														
	210					215					220																		
Ala	Ser	Leu	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val														
	225				230						235			240															
Ala	Arg	Leu	Ser	Gln	Arg	Phe	Pro	Lys	Ala	Glu	Phe	Ala	Glu	Val	Ser														
			245					250					255																
Lys	Leu	Val	Thr	Asp	Leu	Thr	Lys	Val	His	Thr	Glu	Cys	Cys	His	Gly														
		260					265						270																
Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Asp	Leu	Ala	Lys	Tyr	Ile														
	275						280					285																	
Cys	Glu	Asn	Gln	Asp	Ser	Ile	Ser	Ser	Lys	Leu	Lys	Glu	Cys	Cys	Glu														
	290					295					300																		
Lys	Pro	Leu	Leu	Glu	Lys	Ser	His	Cys	Ile	Ala	Glu	Val	Glu	Asn	Asp														
	305				310						315			320															
Glu	Met	Pro	Ala	Asp	Leu	Pro	Ser	Leu	Ala	Ala	Asp	Phe	Val	Glu	Ser														
			325					330					335																
Lys	Asp	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly														
		340					345						350																
Met	Phe	Leu	Tyr	Glu	Tyr	Ala	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Val														
	355						360						365																
Leu	Leu	Leu	Arg	Leu	Ala	Lys	Thr	Tyr	Glu	Thr	Thr	Leu	Glu	Lys	Cys														
	370					375						380																	
Cys	Ala	Ala	Ala	Asp	Pro	His	Glu	Cys	Tyr	Ala	Lys	Val	Phe	Asp	Glu														
	385				390				395					400															
Phe	Lys	Pro	Leu	Val	Glu	Glu	Pro	Gln	Asn	Leu	Ile	Lys	Gln	Asn	Cys														
			405					410					415																
Glu	Leu	Phe	Glu	Gln	Leu	Gly	Glu	Tyr	Lys	Phe	Gln	Asn	Ala	Leu	Leu														
		420					425						430																
Val	Arg	Tyr	Thr	Lys	Lys	Val	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val														
	435						440						445																
Glu	Val	Ser	Arg	Asn	Leu	Gly	Lys	Val	Gly	Ser	Lys	Cys	Cys	Lys	His														
	450					455			460																				
Pro	Glu	Ala	Lys	Arg	Met	Pro	Cys	Ala	Glu	Asp	Tyr	Leu	Ser	Val	Val														

465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Tyr Ala Glu His Lys Ser His Arg Gly Glu Tyr Ser Val Cys Asp
 610 615 620
 Ser Glu Ser Leu Trp Val Thr Asp Lys Ser Ser Ala Ile Asp Ile Arg
 625 630 635 640
 Gly His Gln Val Thr Val Leu Gly Glu Ile Lys Thr Gly Asn Ser Pro
 645 650 655
 Val Lys Gln Tyr Phe Tyr Glu Thr Arg Cys Lys Glu Ala Arg Pro Val
 660 665 670
 Lys Asn Gly Cys Arg Gly Ile Asp Asp Lys His Trp Asn Ser Gln Cys
 675 680 685
 Lys Thr Ser Gln Thr Tyr Val Arg Ala Leu Thr Ser Glu Asn Asn Lys
 690 695 700
 Leu Val Gly Trp Arg Trp Ile Arg Ile Asp Thr Ser Cys Val Cys Ala
 705 710 715 720
 Leu Ser Arg Lys Ile Gly Arg Thr
 725

<210> 254

<211> 728

<212> PRT

<213> Homo sapiens

<400> 254

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Tyr Ala Glu His Lys Ser His Arg
 20 25 30
 Gly Glu Tyr Ser Val Cys Asp Ser Glu Ser Leu Trp Val Thr Asp Lys
 35 40 45
 Ser Ser Ala Ile Asp Ile Arg Gly His Gln Val Thr Val Leu Gly Glu
 50 55 60
 Ile Lys Thr Gly Asn Ser Pro Val Lys Gln Tyr Phe Tyr Glu Thr Arg
 65 70 75 80
 Cys Lys Glu Ala Arg Pro Val Lys Asn Gly Cys Arg Gly Ile Asp Asp
 85 90 95
 Lys His Trp Asn Ser Gln Cys Lys Thr Ser Gln Thr Tyr Val Arg Ala
 100 105 110
 Leu Thr Ser Glu Asn Asn Lys Leu Val Gly Trp Arg Trp Ile Arg Ile
 115 120 125
 Asp Thr Ser Cys Val Cys Ala Leu Ser Arg Lys Ile Gly Arg Thr Asp
 130 135 140
 Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
 145 150 155 160
 Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
 165 170 175
 Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
 180 185 190
 Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
 195 200 205
 Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
 210 215 220
 Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
 225 230 235 240
 Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
 245 250 255
 Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
 260 265 270
 Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
 275 280 285
 His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
 290 295 300

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
 305 310 315 320
 Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
 325 330 335
 Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
 340 345 350
 Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
 355 360 365
 Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
 370 375 380
 His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
 385 390 395 400
 Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
 405 410 415
 Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
 420 425 430
 Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
 435 440 445
 Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
 450 455 460
 Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
 465 470 475 480
 His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
 485 490 495
 Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
 500 505 510
 Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
 515 520 525
 Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
 530 535 540
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 545 550 555 560
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 565 570 575
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 580 585 590
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 595 600 605

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 610 615 620
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 625 630 635 640
 Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
 645 650 655
 Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
 660 665 670
 Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
 675 680 685
 Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
 690 695 700
 Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
 705 710 715 720
 Ala Ser Gln Ala Ala Leu Gly Leu
 725

<210> 255
 <211> 744
 <212> PRT
 <213> Homo sapiens

<400> 255
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430

Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Trp Gly Pro Asp Ala Arg Gly Val Pro Val Ala Asp Gly Glu Phe
 610 615 620
 Ser Ser Glu Gln Val Ala Lys Ala Gly Gly Thr Trp Leu Gly Thr His
 625 630 635 640
 Arg Pro Leu Ala Arg Leu Arg Arg Ala Leu Ser Gly Pro Cys Gln Leu
 645 650 655
 Trp Ser Leu Thr Leu Ser Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser
 660 665 670
 Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Arg Gly
 675 680 685
 Ala Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln Gly Gln Gly
 690 695 700
 Arg Ala His Gly Gly Pro Cys Cys Arg Pro Thr Arg Tyr Thr Asp Val
 705 710 715 720
 Ala Phe Leu Asp Asp Arg His Arg Trp Gln Arg Leu Pro Gln Leu Ser
 725 730 735

Ala Ala Ala Cys Gly Cys Gly Gly
740

<210> 256

<211> 744

<212> PRT

<213> Homo sapiens

<400> 256

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Trp Gly Pro Asp Ala Arg Gly Val
20 25 30

Pro Val Ala Asp Gly Glu Phe Ser Ser Glu Gln Val Ala Lys Ala Gly
35 40 45

Gly Thr Trp Leu Gly Thr His Arg Pro Leu Ala Arg Leu Arg Arg Ala
50 55 60

Leu Ser Gly Pro Cys Gln Leu Trp Ser Leu Thr Leu Ser Val Ala Glu
65 70 75 80

Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys
85 90 95

Ala Gly Ser Cys Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala Leu
100 105 110

Ala Arg Leu Gln Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys Arg
115 120 125

Pro Thr Arg Tyr Thr Asp Val Ala Phe Leu Asp Asp Arg His Arg Trp
130 135 140

Gln Arg Leu Pro Gln Leu Ser Ala Ala Ala Cys Gly Cys Gly Gly Asp
145 150 155 160

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
165 170 175

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
180 185 190

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
195 200 205

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
210 215 220

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
225 230 235 240

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu

202

545 550 555 560
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
 565 570 575
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
 580 585 590
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
 595 600 605
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
 610 615 620
 Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
 625 630 635 640
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
 645 650 655
 Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
 660 665 670
 Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
 675 680 685
 Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
 690 695 700
 Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
 705 710 715 720
 Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
 725 730 735
 Ala Ser Gln Ala Ala Leu Gly Leu
 740

<210> 257

<211> 790

<212> PRT

<213> Homo sapiens

<400> 257

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365

Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro
 610 615 620
 Pro Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr
 625 630 635 640
 Ala Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser
 645 650 655
 Arg Pro Ala Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly
 660 665 670

Gly Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala
675 680 685

Gly Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala
690 695 700

Leu Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys
705 710 715 720

Ser Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala
725 730 735

Ser Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro
740 745 750

Val Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe
755 760 765

Met Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr
770 775 780

Ala Cys Gly Cys Leu Gly
785 790

<210> 258

<211> 790

<212> PRT

<213> Homo sapiens

<400> 258

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Ser Leu Gly Ser Ala Pro Arg Ser
20 25 30

Pro Ala Pro Arg Glu Gly Pro Pro Pro Val Leu Ala Ser Pro Ala Gly
35 40 45

His Leu Pro Gly Gly Arg Thr Ala Arg Trp Cys Ser Gly Arg Ala Arg
50 55 60

Arg Pro Pro Pro Gln Pro Ser Arg Pro Ala Pro Pro Pro Pro Ala Pro
65 70 75 80

Pro Ser Ala Leu Pro Arg Gly Gly Arg Ala Ala Arg Ala Gly Gly Pro
85 90 95

Gly Ser Arg Ala Arg Ala Ala Gly Ala Arg Gly Cys Arg Leu Arg Ser
100 105 110

Gln Leu Val Pro Val Arg Ala Leu Gly Leu Gly His Arg Ser Asp Glu
115 120 125

Leu Val Arg Phe Arg Phe Cys Ser Gly Ser Cys Arg Arg Ala Arg Ser
 130 135 140
 Pro His Asp Leu Ser Leu Ala Ser Leu Leu Gly Ala Gly Ala Leu Arg
 145 150 155 160
 Pro Pro Pro Gly Ser Arg Pro Val Ser Gln Pro Cys Cys Arg Pro Thr
 165 170 175
 Arg Tyr Glu Ala Val Ser Phe Met Asp Val Asn Ser Thr Trp Arg Thr
 180 185 190
 Val Asp Arg Leu Ser Ala Thr Ala Cys Gly Cys Leu Gly Asp Ala His
 195 200 205
 Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
 210 215 220
 Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
 225 230 235 240
 Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
 245 250 255
 Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
 260 265 270
 Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Gly Thr
 275 280 285
 Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
 290 295 300
 Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 305 310 315 320
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 325 330 335
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
 340 345 350
 Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 355 360 365
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 370 375 380
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 385 390 395 400
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 405 410 415
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 420 425 430

Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 435 440 445
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 450 455 460
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 465 470 475 480
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 485 490 495
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 500 505 510
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 515 520 525
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 530 535 540
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 545 550 555 560
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 565 570 575
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 580 585 590
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 595 600 605
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 610 615 620
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 625 630 635 640
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 645 650 655
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 660 665 670
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 675 680 685
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 690 695 700
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 705 710 715 720
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 725 730 735

Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 740 745 750
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 755 760 765
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 770 775 780
 Gln Ala Ala Leu Gly Leu
 785 790

<210> 259
 <211> 790
 <212> PRT
 <213> Homo sapiens

<400> 259
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
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 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu

195	200	205
Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys 210 215 220		
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val 225 230 235 240		
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser 245 250 255		
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly 260 265 270		
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile 275 280 285		
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu 290 295 300		
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp 305 310 315 320		
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser 325 330 335		
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly 340 345 350		
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val 355 360 365		
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys 370 375 380		
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu 385 390 395 400		
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys 405 410 415		
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu 420 425 430		
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val 435 440 445		
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His 450 455 460		
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val 465 470 475 480		
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg 485 490 495		
Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe		

500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro
 610 615 620
 Pro Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr
 625 630 635 640
 Ala Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser
 645 650 655
 Arg Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly
 660 665 670
 Gly Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala
 675 680 685
 Gly Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala
 690 695 700
 Leu Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys
 705 710 715 720
 Ser Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala
 725 730 735
 Ser Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro
 740 745 750
 Val Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe
 755 760 765
 Met Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr
 770 775 780
 Ala Cys Gly Cys Leu Gly
 785 790

<210> 260

<211> 790

<212> PRT

<213> Homo sapiens

<400> 260

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Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1              5              10              15

Tyr Ser Arg Ser Leu Asp Lys Arg Ser Leu Gly Ser Ala Pro Arg Ser
      20              25              30

Pro Ala Pro Arg Glu Gly Pro Pro Pro Val Leu Ala Ser Pro Ala Gly
      35              40              45

His Leu Pro Gly Gly Arg Thr Ala Arg Trp Cys Ser Gly Arg Ala Arg
      50              55              60

Arg Pro Pro Pro Gln Pro Ser Arg Pro Ala Pro Pro Pro Pro Ala Pro
      65              70              75              80

Pro Ser Ala Leu Pro Arg Gly Gly Arg Ala Ala Arg Ala Gly Gly Pro
      85              90              95

Gly Ser Arg Ala Arg Ala Ala Gly Ala Arg Gly Cys Arg Leu Arg Ser
      100             105             110

Gln Leu Val Pro Val Arg Ala Leu Gly Leu Gly His Arg Ser Asp Glu
      115             120             125

Leu Val Arg Phe Arg Phe Cys Ser Gly Ser Cys Arg Arg Ala Arg Ser
      130             135             140

Pro His Asp Leu Ser Leu Ala Ser Leu Leu Gly Ala Gly Ala Leu Arg
      145             150             155             160

Pro Pro Pro Gly Ser Arg Pro Val Ser Gln Pro Cys Cys Arg Pro Thr
      165             170             175

Arg Tyr Glu Ala Val Ser Phe Met Asp Val Asn Ser Thr Trp Arg Thr
      180             185             190

Val Asp Arg Leu Ser Ala Thr Ala Cys Gly Cys Leu Gly Asp Ala His
      195             200             205

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
      210             215             220

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
      225             230             235             240

Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
      245             250             255

Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
      260             265             270

```

Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
 275 280 285
 Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
 290 295 300
 Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 305 310 315 320
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 325 330 335
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
 340 345 350
 Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 355 360 365
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 370 375 380
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 385 390 395 400
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 405 410 415
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 420 425 430
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 435 440 445
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 450 455 460
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 465 470 475 480
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 485 490 495
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 500 505 510
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 515 520 525
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 530 535 540
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 545 550 555 560
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 565 570 575

Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
580 585 590

Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
595 600 605

Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
610 615 620

Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
625 630 635 640

Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
645 650 655

Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
660 665 670

Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
675 680 685

Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
690 695 700

Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
705 710 715 720

Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
725 730 735

Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
740 745 750

Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
755 760 765

Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
770 775 780

Gln Ala Ala Leu Gly Leu
785 790

<210> 261

<211> 790

<212> PRT

<213> Homo sapiens

<400> 261

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335

Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro
 610 615 620
 Pro Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr
 625 630 635 640

Ala Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser
645 650 655

Arg Pro Ala Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly
660 665 670

Gly Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala
675 680 685

Gly Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala
690 695 700

Leu Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys
705 710 715 720

Ser Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala
725 730 735

Ser Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro
740 745 750

Val Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe
755 760 765

Met Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr
770 775 780

Ala Cys Gly Cys Leu Gly
785 790

<210> 262
<211> 790
<212> PRT
<213> Homo sapiens

<400> 262
Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Ser Leu Gly Ser Ala Pro Arg Ser
20 25 30

Pro Ala Pro Arg Glu Gly Pro Pro Pro Val Leu Ala Ser Pro Ala Gly
35 40 45

His Leu Pro Gly Gly Arg Thr Ala Arg Trp Cys Ser Gly Arg Ala Arg
50 55 60

Arg Pro Pro Pro Gln Pro Ser Arg Pro Ala Pro Pro Pro Ala Pro
65 70 75 80

Pro Ser Ala Leu Pro Arg Gly Gly Arg Ala Ala Arg Ala Gly Gly Pro
85 90 95

Gly Ser Arg Ala Arg Ala Ala Gly Ala Arg Gly Cys Arg Leu Arg Ser

100					105					110						
Gln	Leu	Val	Pro	Val	Arg	Ala	Leu	Gly	Leu	Gly	His	Arg	Ser	Asp	Glu	
115					120					125						
Leu	Val	Arg	Phe	Arg	Phe	Cys	Ser	Gly	Ser	Cys	Arg	Arg	Ala	Arg	Ser	
130					135					140						
Pro	His	Asp	Leu	Ser	Leu	Ala	Ser	Leu	Leu	Gly	Ala	Gly	Ala	Leu	Arg	
145					150					155					160	
Pro	Pro	Pro	Gly	Ser	Arg	Pro	Val	Ser	Gln	Pro	Cys	Cys	Arg	Pro	Thr	
165					170					175						
Arg	Tyr	Glu	Ala	Val	Ser	Phe	Met	Asp	Val	Asn	Ser	Thr	Trp	Arg	Thr	
180					185					190						
Val	Asp	Arg	Leu	Ser	Ala	Thr	Ala	Cys	Gly	Cys	Leu	Gly	Asp	Ala	His	
195					200					205						
Lys	Ser	Glu	Val	Ala	His	Arg	Phe	Lys	Asp	Leu	Gly	Glu	Glu	Asn	Phe	
210					215					220						
Lys	Ala	Leu	Val	Leu	Ile	Ala	Phe	Ala	Gln	Tyr	Leu	Gln	Gln	Cys	Pro	
225					230					235					240	
Phe	Glu	Asp	His	Val	Lys	Leu	Val	Asn	Glu	Val	Thr	Glu	Phe	Ala	Lys	
245					250					255						
Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala	Glu	Asn	Cys	Asp	Lys	Ser	Leu	His	
260					265					270						
Thr	Leu	Phe	Gly	Asp	Lys	Leu	Cys	Thr	Val	Ala	Thr	Leu	Arg	Glu	Thr	
275					280					285						
Tyr	Gly	Glu	Met	Ala	Asp	Cys	Cys	Ala	Lys	Gln	Glu	Pro	Glu	Arg	Asn	
290					295					300						
Glu	Cys	Phe	Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Asn	Leu	Pro	Arg	Leu	
305					310					315					320	
Val	Arg	Pro	Glu	Val	Asp	Val	Met	Cys	Thr	Ala	Phe	His	Asp	Asn	Glu	
325					330					335						
Glu	Thr	Phe	Leu	Lys	Lys	Tyr	Leu	Tyr	Glu	Ile	Ala	Arg	Arg	His	Pro	
340					345					350						
Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Phe	Phe	Ala	Lys	Arg	Tyr	Lys	Ala	
355					360					365						
Ala	Phe	Thr	Glu	Cys	Cys	Gln	Ala	Ala	Asp	Lys	Ala	Ala	Cys	Leu	Leu	
370					375					380						
Pro	Lys	Leu	Asp	Glu	Leu	Arg	Asp	Glu	Gly	Lys	Ala	Ser	Ser	Ala	Lys	
385					390					395					400	
Gln	Arg	Leu	Lys	Cys	Ala	Ser	Leu	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	

405 410 415
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 420 425 430
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 435 440 445
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 450 455 460
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 465 470 475 480
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 485 490 495
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 500 505 510
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 515 520 525
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 530 535 540
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 545 550 555 560
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 565 570 575
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 580 585 590
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 595 600 605
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 610 615 620
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 625 630 635 640
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 645 650 655
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 660 665 670
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 675 680 685
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 690 695 700
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr

705 710 715 720
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 725 730 735
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 740 745 750
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 755 760 765
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 770 775 780
 Gln Ala Ala Leu Gly Leu
 785 790

<210> 263
 <211> 739
 <212> PRT
 <213> Homo sapiens

<400> 263
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480

Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala
 610 615 620
 Val Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val
 625 630 635 640
 Asp Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala
 645 650 655
 Gly Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala
 660 665 670
 Asp Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Gly Cys Arg
 675 680 685
 Gly Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser
 690 695 700
 Tyr Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg
 705 710 715 720
 Trp Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr
 725 730 735
 Gly Arg Ala

<210> 264

<211> 739

<212> PRT

<213> Homo sapiens

<400> 264

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Gly Val Ser Glu Thr Ala Pro Ala
 20 25 30
 Ser Arg Arg Gly Glu Leu Ala Val Cys Asp Ala Val Ser Gly Trp Val
 35 40 45
 Thr Asp Arg Arg Thr Ala Val Asp Leu Arg Gly Arg Glu Val Glu Val
 50 55 60
 Leu Gly Glu Val Pro Ala Ala Gly Gly Ser Pro Leu Arg Gln Tyr Phe
 65 70 75 80
 Phe Glu Thr Arg Cys Lys Ala Asp Asn Ala Glu Glu Gly Gly Pro Gly
 85 90 95
 Ala Gly Gly Gly Gly Cys Arg Gly Val Asp Arg Arg His Trp Val Ser
 100 105 110
 Glu Cys Lys Ala Lys Gln Ser Tyr Val Arg Ala Leu Thr Ala Asp Ala
 115 120 125
 Gln Gly Arg Val Gly Trp Arg Trp Ile Arg Ile Asp Thr Ala Cys Val
 130 135 140
 Cys Thr Leu Leu Ser Arg Thr Gly Arg Ala Asp Ala His Lys Ser Glu
 145 150 155 160
 Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu
 165 170 175
 Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp
 180 185 190
 His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val
 195 200 205
 Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe
 210 215 220
 Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu
 225 230 235 240
 Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
 245 250 255
 Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro
 260 265 270
 Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe
 275 280 285

Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr
 290 295 300
 Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr
 305 310 315 320
 Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu
 325 330 335
 Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu
 340 345 350
 Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
 355 360 365
 Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu
 370 375 380
 Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys
 385 390 395 400
 His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys
 405 410 415
 Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys
 420 425 430
 Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu
 435 440 445
 Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val
 450 455 460
 Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
 465 470 475 480
 Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser
 485 490 495
 Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu
 500 505 510
 Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe
 515 520 525
 Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln
 530 535 540
 Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala
 545 550 555 560
 Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr
 565 570 575
 Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys
 580 585 590

Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser
 595 600 605
 Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
 610 615 620
 Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
 625 630 635 640
 Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
 645 650 655
 Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
 660 665 670
 Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
 675 680 685
 His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp
 690 695 700
 Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
 705 710 715 720
 Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
 725 730 735
 Leu Gly Leu

<210> 265

<211> 637

<212> PRT

<213> Homo sapiens

<400> 265

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala

100	105	110
Asp Cys Cys Ala Lys Gln Glu 115	Pro Glu Arg Asn Glu Cys 120	Phe Leu Gln 125
His Lys Asp Asp Asn Pro 130	Asn Leu Pro Arg Leu Val 135	Arg Pro Glu Val 140
Asp Val Met Cys Thr Ala Phe 145	His Asp Asn Glu Glu Thr 150	Phe Leu Lys 155
Lys Tyr Leu Tyr Glu Ile Ala Arg 165	Arg His Pro Tyr Phe Tyr 170	Ala Pro 175
Glu Leu Leu Phe Phe Ala Lys Arg 180	Tyr Lys Ala Ala Phe Thr 185	Glu Cys 190
Cys Gln Ala Ala Asp Lys Ala 195	Ala Cys Leu Leu Pro Lys 200	Leu Asp Glu 205
Leu Arg Asp Glu Gly Lys Ala 210	Ser Ser Ala Lys Gln Arg 215	Leu Lys Cys 220
Ala Ser Leu Gln Lys Phe Gly 225	Glu Arg Ala Phe Lys Ala 230	Trp Ala Val 235
Ala Arg Leu Ser Gln Arg Phe 245	Pro Lys Ala Glu Phe Ala 250	Glu Val Ser 255
Lys Leu Val Thr Asp Leu Thr 260	Lys Val His Thr Glu Cys 265	Cys His Gly 270
Asp Leu Leu Glu Cys Ala Asp 275	Asp Arg Ala Asp Leu Ala 280	Lys Tyr Ile 285
Cys Glu Asn Gln Asp Ser Ile 290	Ser Ser Lys Leu Lys Glu 295	Cys Cys Glu 300
Lys Pro Leu Leu Glu Lys Ser 305	His Cys Ile Ala Glu Val 310	Glu Asn Asp 315
Glu Met Pro Ala Asp Leu Pro 325	Ser Leu Ala Ala Asp Phe 330	Val Glu Ser 335
Lys Asp Val Cys Lys Asn Tyr 340	Ala Glu Ala Lys Asp Val 345	Phe Leu Gly 350
Met Phe Leu Tyr Glu Tyr Ala 355	Arg Arg His Pro Asp Tyr 360	Ser Val Val 365
Leu Leu Leu Arg Leu Ala Lys 370	Thr Tyr Glu Thr Thr Leu 375	Glu Lys Cys 380
Cys Ala Ala Ala Asp Pro His 385	Glu Cys Tyr Ala Lys Val 390	Phe Asp Glu 395
Phe Lys Pro Leu Val Glu Glu 400	Pro Gln Asn Leu Ile Lys 405	Gln Asn Cys 410

405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys
 610 615 620
 Gln Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
 625 630 635

<210> 266

<211> 637

<212> PRT

<213> Homo sapiens

<400> 266

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Ala Val Phe Thr Asp
 20 25 30

Asn Tyr Thr Arg Leu Arg Lys Gln Met Ala Val Lys Lys Tyr Leu Asn
 35 40 45
 Ser Ile Leu Asn Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys
 50 55 60
 Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala
 65 70 75 80
 Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn
 85 90 95
 Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu
 100 105 110
 Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr
 115 120 125
 Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala
 130 135 140
 Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp
 145 150 155 160
 Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys
 165 170 175
 Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr
 180 185 190
 Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe
 195 200 205
 Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala
 210 215 220
 Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu
 225 230 235 240
 Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln
 245 250 255
 Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser
 260 265 270
 Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr
 275 280 285
 Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu
 290 295 300
 Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln
 305 310 315 320
 Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu
 325 330 335

Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala
 340 345 350
 Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys
 355 360 365
 Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr
 370 375 380
 Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg
 385 390 395 400
 Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala
 405 410 415
 Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu
 420 425 430
 Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu
 435 440 445
 Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr
 450 455 460
 Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg
 465 470 475 480
 Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys
 485 490 495
 Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu
 500 505 510
 Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys
 515 520 525
 Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu
 530 535 540
 Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr
 545 550 555 560
 Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys
 565 570 575
 Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr
 580 585 590
 Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu
 595 600 605
 Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
 610 615 620
 Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 625 630 635

<210> 267

<211> 636

<212> PRT

<213> Homo sapiens

<400> 267

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Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1              5              10              15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
      20              25              30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
      35              40              45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
      50              55              60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
      65              70              75              80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
      85              90              95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
      100              105              110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
      115              120              125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
      130              135              140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
      145              150              155              160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
      165              170              175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
      180              185              190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
      195              200              205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
      210              215              220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
      225              230              235              240

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
      245              250              255

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Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575

Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590

Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605

Leu His Ser Asp Gly Thr Phe Thr Ser Glu Leu Ser Arg Leu Arg Glu
 610 615 620

Gly Ala Arg Leu Gln Arg Leu Leu Gln Gly Leu Val
 625 630 635

<210> 268

<211> 636

<212> PRT

<213> Homo sapiens

<400> 268

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Asp Gly Thr Phe Thr Ser
 20 25 30

Glu Leu Ser Arg Leu Arg Glu Gly Ala Arg Leu Gln Arg Leu Leu Gln
 35 40 45

Gly Leu Val Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
 50 55 60

Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
 65 70 75 80

Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
 85 90 95

Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
 100 105 110

Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
 115 120 125

Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
 130 135 140

Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
 145 150 155 160

Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
 165 170 175

Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu

180					185					190					
Ile	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Phe	Phe
	195						200					205			
Ala	Lys	Arg	Tyr	Lys	Ala	Ala	Phe	Thr	Glu	Cys	Cys	Gln	Ala	Ala	Asp
	210					215					220				
Lys	Ala	Ala	Cys	Leu	Leu	Pro	Lys	Leu	Asp	Glu	Leu	Arg	Asp	Glu	Gly
225				230						235					240
Lys	Ala	Ser	Ser	Ala	Lys	Gln	Arg	Leu	Lys	Cys	Ala	Ser	Leu	Gln	Lys
				245					250					255	
Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln
			260					265					270		
Arg	Phe	Pro	Lys	Ala	Glu	Phe	Ala	Glu	Val	Ser	Lys	Leu	Val	Thr	Asp
		275					280					285			
Leu	Thr	Lys	Val	His	Thr	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys
	290					295					300				
Ala	Asp	Asp	Arg	Ala	Asp	Leu	Ala	Lys	Tyr	Ile	Cys	Glu	Asn	Gln	Asp
305				310						315					320
Ser	Ile	Ser	Ser	Lys	Leu	Lys	Glu	Cys	Cys	Glu	Lys	Pro	Leu	Leu	Glu
				325					330					335	
Lys	Ser	His	Cys	Ile	Ala	Glu	Val	Glu	Asn	Asp	Glu	Met	Pro	Ala	Asp
			340					345					350		
Leu	Pro	Ser	Leu	Ala	Ala	Asp	Phe	Val	Glu	Ser	Lys	Asp	Val	Cys	Lys
		355					360					365			
Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Met	Phe	Leu	Tyr	Glu
	370					375					380				
Tyr	Ala	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Val	Leu	Leu	Leu	Arg	Leu
385				390						395					400
Ala	Lys	Thr	Tyr	Glu	Thr	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Ala	Ala	Asp
				405					410					415	
Pro	His	Glu	Cys	Tyr	Ala	Lys	Val	Phe	Asp	Glu	Phe	Lys	Pro	Leu	Val
			420					425					430		
Glu	Glu	Pro	Gln	Asn	Leu	Ile	Lys	Gln	Asn	Cys	Glu	Leu	Phe	Glu	Gln
		435					440					445			
Leu	Gly	Glu	Tyr	Lys	Phe	Gln	Asn	Ala	Leu	Leu	Val	Arg	Tyr	Thr	Lys
	450					455					460				
Lys	Val	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Val	Ser	Arg	Asn
465				470						475					480
Leu	Gly	Lys	Val	Gly	Ser	Lys	Cys	Cys	Lys	His	Pro	Glu	Ala	Lys	Arg

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<210> 269
<211> 729
<212> PRT
<213> Homo sapiens
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Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415

Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ser Ser Ser His Pro Ile Phe His Arg Gly Glu Phe Ser Val Cys
 610 615 620
 Asp Ser Val Ser Val Trp Val Gly Asp Lys Thr Thr Ala Thr Asp Ile
 625 630 635 640
 Lys Gly Lys Glu Val Met Val Leu Gly Glu Val Asn Ile Asn Asn Ser
 645 650 655
 Val Phe Lys Gln Tyr Phe Phe Glu Thr Lys Cys Arg Asp Pro Asn Pro
 660 665 670
 Val Asp Ser Gly Cys Arg Gly Ile Asp Ser Lys His Trp Asn Ser Tyr
 675 680 685
 Cys Thr Thr Thr His Thr Phe Val Lys Ala Leu Thr Met Asp Gly Lys
 690 695 700
 Gln Ala Ala Trp Arg Phe Ile Arg Ile Asp Thr Ala Cys Val Cys Val
 705 710 715 720

Leu Ser Arg Lys Ala Val Arg Arg Ala
725

<210> 270

<211> 729

<212> PRT

<213> Homo sapiens

<400> 270

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Ser Ser Ser His Pro Ile Phe His
20 25 30

Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly Asp
35 40 45

Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu Gly
50 55 60

Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu Thr
65 70 75 80

Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile Asp
85 90 95

Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val Lys
100 105 110

Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg Ile
115 120 125

Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg Ala
130 135 140

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
145 150 155 160

Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
165 170 175

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
180 185 190

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
195 200 205

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
210 215 220

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
225 230 235 240

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 245 250 255
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 260 265 270
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 275 280 285
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
 290 295 300
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
 305 310 315 320
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
 325 330 335
 Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 340 345 350
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
 355 360 365
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
 370 375 380
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
 385 390 395 400
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
 405 410 415
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
 420 425 430
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
 435 440 445
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
 450 455 460
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
 465 470 475 480
 Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
 485 490 495
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
 500 505 510
 Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
 515 520 525
 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
 530 535 540

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
 545 550 555 560
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
 565 570 575
 Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
 580 585 590
 Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
 595 600 605
 Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
 610 615 620
 Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
 625 630 635 640
 Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
 645 650 655
 Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
 660 665 670
 Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
 675 680 685
 Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
 690 695 700
 Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
 705 710 715 720
 Ala Ala Ser Gln Ala Ala Leu Gly Leu
 725

<210> 271
 <211> 729
 <212> PRT
 <213> Homo sapiens

<400> 271
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp

240

370	375	380
Cys Ala Ala Ala Asp	Pro His Glu Cys Tyr	Ala Lys Val Phe Asp Glu
385	390	395 400
Phe Lys Pro Leu Val	Glu Glu Pro Gln Asn Leu Ile	Lys Gln Asn Cys
405	410	415
Glu Leu Phe Glu Gln Leu Gly	Glu Tyr Lys Phe Gln Asn Ala Leu Leu	
420	425	430
Val Arg Tyr Thr Lys Lys Val	Pro Gln Val Ser Thr Pro Thr Leu Val	
435	440	445
Glu Val Ser Arg Asn Leu Gly	Lys Val Gly Ser Lys Cys Cys Lys His	
450	455	460
Pro Glu Ala Lys Arg Met	Pro Cys Ala Glu Asp Tyr Leu Ser Val Val	
465	470	475 480
Leu Asn Gln Leu Cys Val Leu His	Glu Lys Thr Pro Val Ser Asp Arg	
485	490	495
Val Thr Lys Cys Cys Thr Glu Ser	Leu Val Asn Arg Arg Pro Cys Phe	
500	505	510
Ser Ala Leu Glu Val Asp Glu Thr Tyr Val	Pro Lys Glu Phe Asn Ala	
515	520	525
Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr	Leu Ser Glu Lys Glu	
530	535	540
Arg Gln Ile Lys Lys Gln Thr Ala Leu Val	Glu Leu Val Lys His Lys	
545	550	555 560
Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala		
565	570	575
Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe		
580	585	590
Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly		
595	600	605
Leu Ser Ser Ser His Pro Ile Phe His Arg Gly Glu Phe Ser Val Cys		
610	615	620
Asp Ser Val Ser Val Trp Val Gly Asp Lys Thr Thr Ala Thr Asp Ile		
625	630	635 640
Lys Gly Lys Glu Val Met Val Leu Gly Glu Val Asn Ile Asn Asn Ser		
645	650	655
Val Phe Lys Gln Tyr Phe Phe Glu Thr Lys Cys Arg Asp Pro Asn Pro		
660	665	670
Val Asp Ser Gly Cys Arg Gly Ile Asp Ser Lys His Trp Asn Ser Tyr		

675 680 685
 Cys Thr Thr Thr His Thr Phe Val Lys Ala Leu Thr Met Asp Gly Lys
 690 695 700
 Gln Ala Ala Trp Arg Phe Ile Arg Ile Asp Thr Ala Cys Val Cys Val
 705 710 715 720
 Leu Ser Arg Lys Ala Val Arg Arg Ala
 725

 <210> 272
 <211> 729
 <212> PRT
 <213> Homo sapiens

 <400> 272
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ser Ser Ser His Pro Ile Phe His
 20 25 30
 Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly Asp
 35 40 45
 Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu Gly
 50 55 60
 Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu Thr
 65 70 75 80
 Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile Asp
 85 90 95
 Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val Lys
 100 105 110
 Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg Ile
 115 120 125
 Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg Ala
 130 135 140
 Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
 145 150 155 160
 Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
 165 170 175
 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
 180 185 190
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
 195 200 205

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 210 215 220
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
 225 230 235 240
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 245 250 255
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 260 265 270
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 275 280 285
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
 290 295 300
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
 305 310 315 320
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
 325 330 335
 Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 340 345 350
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
 355 360 365
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
 370 375 380
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
 385 390 395 400
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
 405 410 415
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
 420 425 430
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
 435 440 445
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
 450 455 460
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
 465 470 475 480
 Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
 485 490 495
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
 500 505 510

Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
 515 520 525
 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
 530 535 540
 Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
 545 550 555 560
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
 565 570 575
 Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
 580 585 590
 Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
 595 600 605
 Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
 610 615 620
 Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
 625 630 635 640
 Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
 645 650 655
 Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
 660 665 670
 Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
 675 680 685
 Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
 690 695 700
 Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
 705 710 715 720
 Ala Ala Ser Gln Ala Ala Leu Gly Leu
 725

<210> 273

<211> 678

<212> PRT

<213> Homo. sapiens

<400> 273

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335

Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Arg Ser Leu Gln Asp Thr Glu Glu Lys Ser Arg Ser Phe Ser Ala
 610 615 620
 Ser Gln Ala Asp Pro Leu Ser Asp Pro Asp Gln Met Asn Glu Asp Lys
 625 630 635 640

Arg His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp
645 650 655

Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg
660 665 670

Asn Arg Asn Asn Ile Ala
675

<210> 274

<211> 678

<212> PRT

<213> Homo sapiens

<400> 274

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Arg Ser Leu Gln Asp Thr Glu Glu
20 25 30

Lys Ser Arg Ser Phe Ser Ala Ser Gln Ala Asp Pro Leu Ser Asp Pro
35 40 45

Asp Gln Met Asn Glu Asp Lys Arg His Ser Gln Gly Thr Phe Thr Ser
50 55 60

Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln
65 70 75 80

Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala Asp Ala His
85 90 95

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
100 105 110

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
115 120 125

Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
130 135 140

Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
145 150 155 160

Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
165 170 175

Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
180 185 190

Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
195 200 205

Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu

210	215	220
Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro 225 230 235 240		
Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala 245 250 255		
Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu 260 265 270		
Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys 275 280 285		
Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe 290 295 300		
Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu 305 310 315 320		
Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr 325 330 335		
Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp 340 345 350		
Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu 355 360 365		
Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala 370 375 380		
Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala 385 390 395 400		
Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys 405 410 415		
Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro 420 425 430		
Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr 435 440 445		
Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala 450 455 460		
Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu 465 470 475 480		
Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe 485 490 495		
Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser 500 505 510		
Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser		

515 520 525
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 530 535 540
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 545 550 555 560
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 565 570 575
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 580 585 590
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 595 600 605
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 610 615 620
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 625 630 635 640
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 645 650 655
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 660 665 670
 Gln Ala Ala Leu Gly Leu
 675

<210> 275
 <211> 646
 <212> PRT
 <213> Homo sapiens

<400> 275
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400

Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp
 610 615 620
 Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg
 625 630 635 640
 Asn Arg Asn Asn Ile Ala
 645

<210> 276

<211> 646

<212> PRT

<213> Homo sapiens

<400> 276

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg His Ser Gln Gly Thr Phe Thr Ser
 20 25 30
 Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln
 35 40 45
 Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala Asp Ala His
 50 55 60
 Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
 65 70 75 80
 Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
 85 90 95
 Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
 100 105 110
 Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
 115 120 125
 Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
 130 135 140
 Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
 145 150 155 160
 Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 165 170 175
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 180 185 190
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
 195 200 205
 Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 210 215 220
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 225 230 235 240
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 245 250 255
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 260 265 270
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 275 280 285
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 290 295 300

Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 305 310 315 320
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 325 330 335
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 340 345 350
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 355 360 365
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 370 375 380
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 385 390 395 400
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 405 410 415
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 420 425 430
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 435 440 445
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 450 455 460
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 465 470 475 480
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 485 490 495
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 500 505 510
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 515 520 525
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 530 535 540
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 545 550 555 560
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 565 570 575
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 580 585 590
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 595 600 605

Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
610 615 620

Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
625 630 635 640

Gln Ala Ala Leu Gly Leu
645

<210> 277

<211> 636

<212> PRT

<213> Homo sapiens

<400> 277

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys

210	215	220
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val 225 230 235 240		
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser 245 250 255		
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly 260 265 270		
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile 275 280 285		
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu 290 295 300		
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp 305 310 315 320		
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser 325 330 335		
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly 340 345 350		
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val 355 360 365		
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys 370 375 380		
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu 385 390 395 400		
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys 405 410 415		
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu 420 425 430		
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val 435 440 445		
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His 450 455 460		
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val 465 470 475 480		
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg 485 490 495		
Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe 500 505 510		
Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala		

515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu His Ala Asp Gly Val Phe Thr Ser Asp Phe Ser Lys Leu Leu Gly
 610 615 620
 Gln Leu Ser Ala Lys Lys Tyr Leu Glu Ser Leu Met
 625 630 635

<210> 278

<211> 636

<212> PRT

<213> Homo sapiens

<400> 278

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg His Ala Asp Gly Val Phe Thr Ser
 20 25 30
 Asp Phe Ser Lys Leu Leu Gly Gln Leu Ser Ala Lys Lys Tyr Leu Glu
 35 40 45
 Ser Leu Met Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
 50 55 60
 Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
 65 70 75 80
 Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
 85 90 95
 Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
 100 105 110
 Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
 115 120 125
 Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
 130 135 140

Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
 145 150 155 160
 Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
 165 170 175
 Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu
 180 185 190
 Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe
 195 200 205
 Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp
 210 215 220
 Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly
 225 230 235 240
 Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys
 245 250 255
 Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
 260 265 270
 Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp
 275 280 285
 Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys
 290 295 300
 Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp
 305 310 315 320
 Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu
 325 330 335
 Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp
 340 345 350
 Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys
 355 360 365
 Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu
 370 375 380
 Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu
 385 390 395 400
 Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp
 405 410 415
 Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val
 420 425 430
 Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
 435 440 445

Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
 450 455 460
 Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
 465 470 475 480
 Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
 485 490 495
 Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
 500 505 510
 Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
 515 520 525
 Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
 530 535 540
 Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
 545 550 555 560
 His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
 565 570 575
 Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
 580 585 590
 Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
 595 600 605
 Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
 610 615 620
 Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 625 630 635

<210> 279

<211> 634

<212> PRT

<213> Homo sapiens

<400> 279

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365

Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Asn Leu His Phe Cys Gln Leu Arg Cys Lys Ser Leu Gly Leu Leu
 610 615 620
 Gly Lys Cys Ala Gly Ser Cys Ala Cys Val
 625 630

<210> 280

<211> 634

<212> PRT

<213> Homo sapiens

<400> 280

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Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1           5           10           15

Tyr Ser Arg Ser Leu Asp Lys Arg Asn Leu His Phe Cys Gln Leu Arg
      20           25           30

Cys Lys Ser Leu Gly Leu Leu Gly Lys Cys Ala Gly Ser Cys Ala Cys
      35           40           45

Val Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly
 50           55           60

Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu
 65           70           75           80

Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr
      85           90           95

Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp
      100           105           110

Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr
      115           120           125

Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu
      130           135           140

Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn
      145           150           155           160

Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe
      165           170           175

His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala
      180           185           190

Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys
      195           200           205

Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala
      210           215           220

Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala
      225           230           235           240

Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly
      245           250           255

Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe
      260           265           270

Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr
      275           280           285

Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp

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290 295 300
 Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile
 305 310 315 320
 Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser
 325 330 335
 His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro
 340 345 350
 Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr
 355 360 365
 Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala
 370 375 380
 Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys
 385 390 395 400
 Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His
 405 410 415
 Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu
 420 425 430
 Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly
 435 440 445
 Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val
 450 455 460
 Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly
 465 470 475 480
 Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro
 485 490 495
 Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu
 500 505 510
 His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu
 515 520 525
 Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu
 530 535 540
 Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala
 545 550 555 560
 Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
 565 570 575
 Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln
 580 585 590
 Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys

595 600 605
 Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu
 610 615 620
 Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 625 630

 <210> 281
 <211> 661
 <212> PRT
 <213> Homo sapiens

 <400> 281
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys
 50 55 60
 Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Asp Ala His Lys
 65 70 75 80
 Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys
 85 90 95
 Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe
 100 105 110
 Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr
 115 120 125
 Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr
 130 135 140
 Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr
 145 150 155 160
 Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu
 165 170 175
 Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val
 180 185 190
 Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu
 195 200 205
 Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg His Pro Tyr
 210 215 220

Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala
 225 230 235 240
 Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro
 245 250 255
 Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln
 260 265 270
 Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys
 275 280 285
 Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe
 290 295 300
 Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu
 305 310 315 320
 Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu
 325 330 335
 Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys
 340 345 350
 Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu
 355 360 365
 Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp
 370 375 380
 Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp
 385 390 395 400
 Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp
 405 410 415
 Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr
 420 425 430
 Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys
 435 440 445
 Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile
 450 455 460
 Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln
 465 470 475 480
 Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr
 485 490 495
 Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys
 500 505 510
 Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr
 515 520 525

Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro
 530 535 540
 Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg
 545 550 555 560
 Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys
 565 570 575
 Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu
 580 585 590
 Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu
 595 600 605
 Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met
 610 615 620
 Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys
 625 630 635 640
 Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln
 645 650 655
 Ala Ala Leu Gly Leu
 660

<210> 282
 <211> 665
 <212> PRT
 <213> Homo sapiens

<400> 282
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Lys Val Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly
 50 55 60
 Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val
 65 70 75 80
 Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
 85 90 95
 Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
 100 105 110

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
 115 120 125
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
 130 135 140
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 145 150 155 160
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
 165 170 175
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 180 185 190
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 195 200 205
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 210 215 220
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
 225 230 235 240
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
 245 250 255
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
 260 265 270
 Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 275 280 285
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
 290 295 300
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
 305 310 315 320
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
 325 330 335
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
 340 345 350
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
 355 360 365
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
 370 375 380
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
 385 390 395 400
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
 405 410 415

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
 420 425 430
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
 435 440 445
 Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
 450 455 460
 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
 465 470 475 480
 Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
 485 490 495
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
 500 505 510
 Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
 515 520 525
 Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
 530 535 540
 Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
 545 550 555 560
 Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
 565 570 575
 Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
 580 585 590
 Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
 595 600 605
 Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
 610 615 620
 Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
 625 630 635 640
 Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
 645 650 655
 Ala Ala Ser Gln Ala Ala Leu Gly Leu
 660 665

<210> 283

<211> 670

<212> PRT

<213> Homo sapiens

<400> 283

Met Trp Trp Arg Leu Trp Trp Leu Leu Leu Leu Leu Leu Leu Trp

1	5	10	15
Pro Met Val Trp Ala Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe	20	25	30
Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys	35	40	45
Val Leu Arg Arg His Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe	50	55	60
Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys	65	70	80
Val Leu Arg Arg His Asp Ala His Lys Ser Glu Val Ala His Arg Phe	85	90	95
Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe	100	105	110
Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val	115	120	125
Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala	130	135	140
Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys	145	150	160
Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys	165	170	175
Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp	180	185	190
Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met	195	200	205
Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu	210	215	220
Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu	225	230	240
Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala	245	250	255
Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp	260	265	270
Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu	275	280	285
Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu	290	295	300
Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val			

305 310 315 320
 Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu
 325 330 335
 Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn
 340 345 350
 Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu
 355 360 365
 Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro
 370 375 380
 Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val
 385 390 395 400
 Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu
 405 410 415
 Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu
 420 425 430
 Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala
 435 440 445
 Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro
 450 455 460
 Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe
 465 470 475 480
 Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr
 485 490 495
 Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser
 500 505 510
 Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala
 515 520 525
 Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln
 530 535 540
 Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys
 545 550 555 560
 Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu
 565 570 575
 Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe
 580 585 590
 Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile
 595 600 605
 Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala

610 615 620
 Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val
 625 630 635 640
 Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu
 645 650 655
 Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 660 665 670

<210> 284
 <211> 663
 <212> PRT
 <213> Homo sapiens

<400> 284
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ser Pro Lys Met Val Gln Gly Ser
 20 25 30
 Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
 35 40 45
 Gly Cys Lys Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg
 50 55 60
 Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Asp Ala
 65 70 75 80
 His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
 85 90 95
 Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
 100 105 110
 Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
 115 120 125
 Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu
 130 135 140
 His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
 145 150 155 160
 Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
 165 170 175
 Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
 180 185 190
 Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
 195 200 205

Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
 210 215 220
 Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
 225 230 235 240
 Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
 245 250 255
 Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
 260 265 270
 Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
 275 280 285
 Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala
 290 295 300
 Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His
 305 310 315 320
 Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
 325 330 335
 Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys
 340 345 350
 Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile
 355 360 365
 Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala
 370 375 380
 Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala
 385 390 395 400
 Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His
 405 410 415
 Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu
 420 425 430
 Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr
 435 440 445
 Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn
 450 455 460
 Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys
 465 470 475 480
 Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val
 485 490 495
 Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly
 500 505 510

Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu
 515 520 525
 Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys
 530 535 540
 Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val
 545 550 555 560
 Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val
 565 570 575
 Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys
 580 585 590
 Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val
 595 600 605
 Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala
 610 615 620
 Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp
 625 630 635 640
 Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
 645 650 655
 Ser Gln Ala Ala Leu Gly Leu
 660

<210> 285
 <211> 68
 <212> PRT
 <213> Homo sapiens

<400> 285
 Ser Arg Gly Pro Tyr His Pro Ser Glu Cys Cys Phe Thr Tyr Thr Thr
 1 5 10 15
 Tyr Lys Ile Pro Arg Gln Arg Ile Met Asp Tyr Tyr Glu Thr Asn Ser
 20 25 30
 Gln Cys Ser Lys Pro Gly Ile Val Phe Ile Thr Lys Arg Gly His Ser
 35 40 45
 Val Cys Thr Asn Pro Ser Asp Lys Trp Val Gln Asp Tyr Ile Lys Asp
 50 55 60
 Met Lys Glu Asn
 65

<210> 286
 <211> 68
 <212> PRT

<213> Homo sapiens

<400> 286

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Ser Arg Gly Pro Tyr His Pro Ser Glu Cys Cys Phe Thr Tyr Thr Thr
 1              5              10              15

Tyr Lys Ile Pro Arg Gln Arg Ile Met Asp Tyr Tyr Glu Thr Asn Ser
      20              25              30

Gln Cys Ser Lys Pro Gly Ile Val Phe Ile Thr Lys Arg Gly His Ser
      35              40              45

Val Cys Thr Asn Pro Ser Asp Lys Trp Val Gln Asp Tyr Ile Lys Asp
      50              55              60

Met Lys Glu Asn
      65

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<210> 287

<211> 66

<212> PRT

<213> Homo sapiens

<400> 287

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Gly Pro Tyr His Pro Ser Glu Cys Cys Phe Thr Tyr Thr Thr Tyr Lys
 1              5              10              15

Ile Pro Arg Gln Arg Ile Met Asp Tyr Tyr Glu Thr Asn Ser Gln Cys
      20              25              30

Ser Lys Pro Gly Ile Val Phe Ile Thr Lys Arg Gly His Ser Val Cys
      35              40              45

Thr Asn Pro Ser Asp Lys Trp Val Gln Asp Tyr Ile Lys Asp Met Lys
      50              55              60

Glu Asn
      65

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<210> 288

<211> 32

<212> PRT

<213> Homo sapiens

<400> 288

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Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1              5              10              15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
      20              25              30

<210> 289
<211> 241
<212> PRT

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<213> Homo sapiens

<400> 289

Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
 1 5 10 15

Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val
 20 25 30

Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
 35 40 45

Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
 50 55 60

Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
 65 70 75 80

Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
 85 90 95

Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg
 100 105 110

Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
 115 120 125

Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu
 130 135 140

Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln
 145 150 155 160

Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp
 165 170 175

Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
 180 185 190

Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
 195 200 205

Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu
 210 215 220

Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr
 225 230 235 240

Lys

<210> 290

<211> 165

<212> PRT

<213> Homo sapiens

<400> 290

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
 100 105 110
 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125
 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
 145 150 155 160
 Leu Arg Ser Lys Glu
 165

<210> 291

<211> 165

<212> PRT

<213> Homo sapiens

<400> 291

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
100 105 110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145 150 155 160

Leu Arg Ser Lys Glu
165

<210> 292

<211> 165

<212> PRT

<213> Homo sapiens

<400> 292

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
85 90 95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
100 105 110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145 150 155 160

Leu Arg Ser Lys Glu
165

<210> 293

<211> 30

<212> PRT

<213> Homo sapiens

<400> 293

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 294

<211> 14

<212> PRT

<213> Homo sapiens

<400> 294

Ala Gly Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys
1 5 10

<210> 295

<211> 30

<212> PRT

<213> Homo sapiens

<400> 295

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 296

<211> 30

<212> PRT

<213> Homo sapiens

<400> 296

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 297

<211> 30

<212> PRT

<213> Homo sapiens

<400> 297

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 298
<211> 32
<212> PRT
<213> Homo sapiens

<400> 298
Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15
Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
20 25 30

<210> 299
<211> 30
<212> PRT
<213> Homo sapiens

<400> 299
His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 300
<211> 30
<212> PRT
<213> Homo sapiens

<400> 300
His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 301
<211> 30
<212> PRT
<213> Homo sapiens

<400> 301
His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 302
<211> 30
<212> PRT
<213> Homo sapiens

<400> 302

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
 20 25 30

<210> 303

<211> 657

<212> PRT

<213> Homo sapiens

<400> 303

Met Asn Ile Phe Tyr Ile Phe Leu Phe Leu Leu Ser Phe Val Gln Gly
 1 5 10 15

Leu Glu His Thr His Arg Arg Gly Ser Leu Asp Lys Arg His Gly Glu
 20 25 30

Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala
 35 40 45

Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Asp Ala His Lys Ser
 50 55 60

Glu Val Ala His Arg Phe Lys Asp Asp Ala His Lys Ser Glu Val Ala
 65 70 75 80

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 85 90 95

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 100 105 110

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 115 120 125

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 130 135 140

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 145 150 155 160

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 165 170 175

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 180 185 190

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 195 200 205

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 210 215 220

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys

225		230		235		240
Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu						
	245			250		255
Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys						
	260		265			270
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val						
	275		280		285	
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser						
	290		295		300	
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly						
305		310		315		320
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile						
	325		330			335
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu						
	340		345			350
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp						
	355		360		365	
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser						
	370		375		380	
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly						
385		390		395		400
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val						
	405		410			415
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys						
	420		425			430
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu						
	435		440		445	
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys						
	450		455		460	
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu						
465		470		475		480
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val						
	485		490			495
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His						
	500		505		510	
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val						
	515		520		525	
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg						

530 535 540
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 545 550 555 560
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 565 570 575
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 580 585 590
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 595 600 605
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 610 615 620
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 625 630 635 640
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 645 650 655

Leu

<210> 304
 <211> 32
 <212> PRT
 <213> Homo sapiens

<400> 304
 Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15
 Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
 20 25 30

<210> 305
 <211> 30
 <212> PRT
 <213> Homo sapiens

<400> 305
 His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15
 Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
 20 25 30

<210> 306
 <211> 30
 <212> PRT

<213> Homo sapiens

<400> 306

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 307

<211> 30

<212> PRT

<213> Homo sapiens

<400> 307

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 308

<211> 30

<212> PRT

<213> Homo sapiens

<400> 308

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 309

<211> 28

<212> PRT

<213> Homo sapiens

<400> 309

Ser Leu Arg Arg Ser Ser Cys Phe Gly Gly Arg Met Asp Arg Ile Gly
1 5 10 15

Ala Gln Ser Gly Leu Gly Cys Asn Ser Phe Arg Tyr
20 25

<210> 310

<211> 30

<212> PRT

<213> Homo sapiens

<400> 310

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
 20 25 30

<210> 311

<211> 30

<212> PRT

<213> Homo sapiens

<400> 311

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
 20 25 30

<210> 312

<211> 30

<212> PRT

<213> Homo sapiens

<400> 312

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
 20 25 30

<210> 313

<211> 34

<212> PRT

<213> Homo sapiens

<400> 313

Ile Lys Pro Glu Ala Pro Gly Glu Asp Ala Ser Pro Glu Glu Leu Asn
 1 5 10 15

Arg Tyr Tyr Ala Ser Leu Arg His Tyr Leu Asn Leu Val Thr Arg Gln
 20 25 30

Arg Tyr

<210> 314

<211> 29

<212> PRT

<213> Homo sapiens

<400> 314

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15

Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys Val Leu
 20 25

<210> 315
<211> 29
<212> PRT
<213> Homo sapiens

<400> 315
Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15
Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys Val Leu
20 25

<210> 316
<211> 34
<212> PRT
<213> Homo sapiens

<400> 316
Ile Lys Pro Glu Ala Pro Gly Glu Asp Ala Ser Pro Glu Glu Leu Asn
1 5 10 15
Arg Tyr Tyr Ala Ser Leu Arg His Tyr Leu Asn Leu Val Thr Arg Gln
20 25 30

Arg Tyr

<210> 317
<211> 32
<212> PRT
<213> Homo sapiens

<400> 317
Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15
Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
20 25 30

<210> 318
<211> 32
<212> PRT
<213> Homo sapiens

<400> 318
Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp

1 5 10 15
 Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
 20 25 30

<210> 319
 <211> 33
 <212> PRT
 <213> Homo sapiens

<400> 319
 His Ala Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn
 1 5 10 15
 Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr
 20 25 30

Asp

<210> 320
 <211> 33
 <212> PRT
 <213> Homo sapiens

<400> 320
 His Ala Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn
 1 5 10 15
 Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr
 20 25 30

Asp

<210> 321
 <211> 26
 <212> PRT
 <213> Homo sapiens

<400> 321
 Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15
 Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys
 20 25

<210> 322
<211> 27
<212> PRT
<213> Homo sapiens

<400> 322
Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Gly Leu Gly Cys Lys
20 25

<210> 323
<211> 28
<212> PRT
<213> Homo sapiens

<400> 323
Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val
20 25

<210> 324
<211> 33
<212> PRT
<213> Homo sapiens

<400> 324
His Gly Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn
1 5 10 15

Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr
20 25 30

Asp

<210> 325
<211> 33
<212> PRT
<213> Homo sapiens

<400> 325
His Gly Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn
1 5 10 15

Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr
20 25 30

Asp

<210> 326
<211> 27
<212> PRT
<213> Homo sapiens

<400> 326
His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln
1 5 10 15
Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu
20 25

<210> 327
<211> 27
<212> PRT
<213> Homo sapiens

<400> 327
His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln
1 5 10 15
Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu
20 25

<210> 328
<211> 38
<212> PRT
<213> Homo sapiens

<400> 328
His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln
1 5 10 15
Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu Gly Lys Arg Tyr Lys
20 25 30
Gln Arg Val Lys Asn Lys
35

<210> 329
<211> 38
<212> PRT
<213> Homo sapiens

<400> 329
His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln
1 5 10 15
Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu Gly Lys Arg Tyr Lys
20 25 30

Gln Arg Val Lys Asn Lys
35

<210> 330

<211> 119

<212> PRT

<213> Homo sapiens

<400> 330

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
1 5 10 15

Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
20 25 30

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
35 40 45

Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
50 55 60

Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
65 70 75 80

Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
85 90 95

Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
100 105 110

Leu Thr Ile Lys Arg Gly Arg
115

<210> 331

<211> 119

<212> PRT

<213> Homo sapiens

<400> 331

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
1 5 10 15

Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
20 25 30

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
35 40 45

Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
50 55 60

Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys

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<210> 332
<211> 119
<212> PRT
<213> Homo sapiens
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<210> 333
<211> 119
<212> PRT
<213> Homo sapiens
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289

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
 35 40 45
 Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
 50 55 60
 Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
 65 70 75 80
 Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
 85 90 95
 Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
 100 105 110
 Leu Thr Ile Lys Arg Gly Arg
 115

<210> 334
 <211> 119
 <212> PRT
 <213> Homo sapiens

<400> 334
 His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
 1 5 10 15
 Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
 20 25 30
 Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
 35 40 45
 Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
 50 55 60
 Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
 65 70 75 80
 Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
 85 90 95
 Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
 100 105 110
 Leu Thr Ile Lys Arg Gly Arg
 115

<210> 335
 <211> 119
 <212> PRT
 <213> Homo sapiens

<400> 335

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
 1 5 10 15
 Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
 20 25 30
 Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
 35 40 45
 Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
 50 55 60
 Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
 65 70 75 80
 Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
 85 90 95
 Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
 100 105 110
 Leu Thr Ile Lys Arg Gly Arg
 115

<210> 336

<211> 192

<212> PRT

<213> Homo sapiens

<400> 336

Phe Pro Leu Pro Ala Gly Lys Arg Pro Pro Glu Ala Pro Ala Glu Asp
 1 5 10 15
 Arg Ser Leu Gly Arg Arg Arg Ala Pro Phe Ala Leu Ser Ser Asp Ser
 20 25 30
 Asn Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val Met Asp Phe
 35 40 45
 Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp Lys Gln Met
 50 55 60
 Ala Val Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala Ala Asn
 65 70 75 80
 Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg Gly Lys Asn
 85 90 95
 Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly
 100 105 110
 Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly
 115 120 125

Ser Cys Asp Ala Ala Glu Thr Thr Tyr Asp Lys Ile Leu Lys Asn Leu
 130 135 140
 Ser Arg Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln Ala Cys Cys
 145 150 155 160
 Arg Pro Ile Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu
 165 170 175
 Val Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys Ile
 180 185 190

<210> 337
 <211> 192
 <212> PRT
 <213> Homo sapiens

<400> 337
 Phe Pro Leu Pro Ala Gly Lys Arg Pro Pro Glu Ala Pro Ala Glu Asp
 1 5 10 15
 Arg Ser Leu Gly Arg Arg Arg Ala Pro Phe Ala Leu Ser Ser Asp Ser
 20 25 30
 Asn Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val Met Asp Phe
 35 40 45
 Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp Lys Gln Met
 50 55 60
 Ala Val Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala Ala Asn
 65 70 75 80
 Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg Gly Lys Asn
 85 90 95
 Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly
 100 105 110
 Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly
 115 120 125
 Ser Cys Asp Ala Ala Glu Thr Thr Tyr Asp Lys Ile Leu Lys Asn Leu
 130 135 140
 Ser Arg Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln Ala Cys Cys
 145 150 155 160
 Arg Pro Ile Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu
 165 170 175
 Val Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys Ile

180

185

190

<210> 338
 <211> 102
 <212> PRT
 <213> Homo sapiens

<400> 338
 Ala Arg Leu Gly Ala Arg Pro Cys Gly Leu Arg Glu Leu Glu Val Arg
 1 5 10 15
 Val Ser Glu Leu Gly Leu Gly Tyr Ala Ser Asp Glu Thr Val Leu Phe
 20 25 30
 Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ala Arg Val Tyr Asp Leu
 35 40 45
 Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Leu Arg Arg Glu Arg Val
 50 55 60
 Arg Ala Gln Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser
 65 70 75 80
 Phe Leu Asp Ala His Ser Arg Tyr His Thr Val His Glu Leu Ser Ala
 85 90 95
 Arg Glu Cys Ala Cys Val
 100

<210> 339
 <211> 102
 <212> PRT
 <213> Homo sapiens

<400> 339
 Ala Arg Leu Gly Ala Arg Pro Cys Gly Leu Arg Glu Leu Glu Val Arg
 1 5 10 15
 Val Ser Glu Leu Gly Leu Gly Tyr Ala Ser Asp Glu Thr Val Leu Phe
 20 25 30
 Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ala Arg Val Tyr Asp Leu
 35 40 45
 Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Leu Arg Arg Glu Arg Val
 50 55 60
 Arg Ala Gln Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser
 65 70 75 80

Phe Leu Asp Ala His Ser Arg Tyr His Thr Val His Glu Leu Ser Ala
 85 90 95

Arg Glu Cys Ala Cys Val
 100

<210> 340
 <211> 119
 <212> PRT
 <213> Homo sapiens

<400> 340
 Tyr Ala Glu His Lys Ser His Arg Gly Glu Tyr Ser Val Cys Asp Ser
 1 5 10 15
 Glu Ser Leu Trp Val Thr Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly
 20 25 30
 His Gln Val Thr Val Leu Gly Glu Ile Lys Thr Gly Asn Ser Pro Val
 35 40 45
 Lys Gln Tyr Phe Tyr Glu Thr Arg Cys Lys Glu Ala Arg Pro Val Lys
 50 55 60
 Asn Gly Cys Arg Gly Ile Asp Asp Lys His Trp Asn Ser Gln Cys Lys
 65 70 75 80
 Thr Ser Gln Thr Tyr Val Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu
 85 90 95
 Val Gly Trp Arg Trp Ile Arg Ile Asp Thr Ser Cys Val Cys Ala Leu
 100 105 110
 Ser Arg Lys Ile Gly Arg Thr
 115

<210> 341
 <211> 119
 <212> PRT
 <213> Homo sapiens

<400> 341
 Tyr Ala Glu His Lys Ser His Arg Gly Glu Tyr Ser Val Cys Asp Ser
 1 5 10 15
 Glu Ser Leu Trp Val Thr Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly
 20 25 30
 His Gln Val Thr Val Leu Gly Glu Ile Lys Thr Gly Asn Ser Pro Val
 35 40 45
 Lys Gln Tyr Phe Tyr Glu Thr Arg Cys Lys Glu Ala Arg Pro Val Lys
 50 55 60

Asn Gly Cys Arg Gly Ile Asp Asp Lys His Trp Asn Ser Gln Cys Lys
 65 70 75 80
 Thr Ser Gln Thr Tyr Val Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu
 85 90 95
 Val Gly Trp Arg Trp Ile Arg Ile Asp Thr Ser Cys Val Cys Ala Leu
 100 105 110
 Ser Arg Lys Ile Gly Arg Thr
 115

<210> 342
 <211> 135
 <212> PRT
 <213> Homo sapiens

<400> 342
 Trp Gly Pro Asp Ala Arg Gly Val Pro Val Ala Asp Gly Glu Phe Ser
 1 5 10 15
 Ser Glu Gln Val Ala Lys Ala Gly Gly Thr Trp Leu Gly Thr His Arg
 20 25 30
 Pro Leu Ala Arg Leu Arg Arg Ala Leu Ser Gly Pro Cys Gln Leu Trp
 35 40 45
 Ser Leu Thr Leu Ser Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu
 50 55 60
 Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Arg Gly Ala
 65 70 75 80
 Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln Gly Gln Gly Arg
 85 90 95
 Ala His Gly Gly Pro Cys Cys Arg Pro Thr Arg Tyr Thr Asp Val Ala
 100 105 110
 Phe Leu Asp Asp Arg His Arg Trp Gln Arg Leu Pro Gln Leu Ser Ala
 115 120 125
 Ala Ala Cys Gly Cys Gly Gly
 130 135

<210> 343
 <211> 135
 <212> PRT
 <213> Homo sapiens

<400> 343
 Trp Gly Pro Asp Ala Arg Gly Val Pro Val Ala Asp Gly Glu Phe Ser

1 5 10 15
 Ser Glu Gln Val Ala Lys Ala Gly Gly Thr Trp Leu Gly Thr His Arg
 20 25 30
 Pro Leu Ala Arg Leu Arg Arg Ala Leu Ser Gly Pro Cys Gln Leu Trp
 35 40 45
 Ser Leu Thr Leu Ser Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu
 50 55 60
 Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Arg Gly Ala
 65 70 75 80
 Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln Gly Gln Gly Arg
 85 90 95
 Ala His Gly Gly Pro Cys Cys Arg Pro Thr Arg Tyr Thr Asp Val Ala
 100 105 110
 Phe Leu Asp Asp Arg His Arg Trp Gln Arg Leu Pro Gln Leu Ser Ala
 115 120 125
 Ala Ala Cys Gly Cys Gly Gly
 130 135

<210> 344
 <211> 181
 <212> PRT
 <213> Homo sapiens

<400> 344
 Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro Pro
 1 5 10 15
 Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr Ala
 20 25 30
 Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser Arg
 35 40 45
 Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly Gly
 50 55 60
 Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala Gly
 65 70 75 80
 Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala Leu
 85 90 95
 Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser
 100 105 110
 Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser
 115 120 125

Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val
 130 135 140
 Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met
 145 150 155 160
 Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr Ala
 165 170 175
 Cys Gly Cys Leu Gly
 180

<210> 345
 <211> 181
 <212> PRT
 <213> Homo sapiens

<400> 345
 Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro Pro
 1 5 10 15
 Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr Ala
 20 25 30
 Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser Arg
 35 40 45
 Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly Gly
 50 55 60
 Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala Gly
 65 70 75 80
 Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala Leu
 85 90 95
 Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser
 100 105 110
 Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser
 115 120 125
 Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val
 130 135 140
 Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met
 145 150 155 160
 Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr Ala
 165 170 175
 Cys Gly Cys Leu Gly
 180

<210> 346

<211> 181

<212> PRT

<213> Homo sapiens

<400> 346

Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro Pro
 1 5 10 15

Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr Ala
 20 25 30

Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser Arg
 35 40 45

Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly Gly
 50 55 60

Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala Gly
 65 70 75 80

Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala Leu
 85 90 95

Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser
 100 105 110

Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser
 115 120 125

Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val
 130 135 140

Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met
 145 150 155 160

Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr Ala
 165 170 175

Cys Gly Cys Leu Gly
 180

<210> 347

<211> 181

<212> PRT

<213> Homo sapiens

<400> 347

Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro Pro
 1 5 10 15

Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr Ala
 20 25 30

Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser Arg
 35 40 45
 Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly Gly
 50 55 60
 Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala Gly
 65 70 75 80
 Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala Leu
 85 90 95
 Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser
 100 105 110
 Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser
 115 120 125
 Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val
 130 135 140
 Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met
 145 150 155 160
 Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr Ala
 165 170 175
 Cys Gly Cys Leu Gly
 180

<210> 348

<211> 181

<212> PRT

<213> Homo sapiens

<400> 348

Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro Pro
 1 5 10 15
 Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr Ala
 20 25 30
 Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser Arg
 35 40 45
 Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly Gly
 50 55 60
 Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala Gly
 65 70 75 80
 Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala Leu
 85 90 95

Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser
 100 105 110
 Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser
 115 120 125
 Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val
 130 135 140
 Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met
 145 150 155 160
 Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr Ala
 165 170 175
 Cys Gly Cys Leu Gly
 180

<210> 349
 <211> 181
 <212> PRT
 <213> Homo sapiens

<400> 349
 Ser Leu Gly Ser Ala Pro Arg Ser Pro Ala Pro Arg Glu Gly Pro Pro
 1 5 10 15
 Pro Val Leu Ala Ser Pro Ala Gly His Leu Pro Gly Gly Arg Thr Ala
 20 25 30
 Arg Trp Cys Ser Gly Arg Ala Arg Arg Pro Pro Pro Gln Pro Ser Arg
 35 40 45
 Pro Ala Pro Pro Pro Pro Ala Pro Pro Ser Ala Leu Pro Arg Gly Gly
 50 55 60
 Arg Ala Ala Arg Ala Gly Gly Pro Gly Ser Arg Ala Arg Ala Ala Gly
 65 70 75 80
 Ala Arg Gly Cys Arg Leu Arg Ser Gln Leu Val Pro Val Arg Ala Leu
 85 90 95
 Gly Leu Gly His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser
 100 105 110
 Gly Ser Cys Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser
 115 120 125
 Leu Leu Gly Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val
 130 135 140
 Ser Gln Pro Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met
 145 150 155 160
 Asp Val Asn Ser Thr Trp Arg Thr Val Asp Arg Leu Ser Ala Thr Ala

165 170 175

Cys Gly Cys Leu Gly
180

<210> 350
<211> 130
<212> PRT
<213> Homo sapiens

<400> 350
Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val
1 5 10 15
Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp
20 25 30
Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly
35 40 45
Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp
50 55 60
Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Cys Arg Gly
65 70 75 80
Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr
85 90 95
Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp
100 105 110
Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly
115 120 125
Arg Ala
130

<210> 351
<211> 130
<212> PRT
<213> Homo sapiens

<400> 351
Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val
1 5 10 15
Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp
20 25 30
Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly
35 40 45
Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp
50 55 60

Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Gly Cys Arg Gly
65 70 75 80

Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr
85 90 95

Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp
100 105 110

Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly
115 120 125

Arg Ala
130

<210> 352

<211> 28

<212> PRT

<213> Homo sapiens

<400> 352

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln
1 5 10 15

Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
20 25

<210> 353

<211> 28

<212> PRT

<213> Homo sapiens

<400> 353

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln
1 5 10 15

Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
20 25

<210> 354

<211> 27

<212> PRT

<213> Homo sapiens

<400> 354

His Ser Asp Gly Thr Phe Thr Ser Glu Leu Ser Arg Leu Arg Glu Gly
1 5 10 15

Ala Arg Leu Gln Arg Leu Leu Gln Gly Leu Val
20 25

<210> 355

<211> 27

<212> PRT

<213> Homo sapiens

<400> 355

His Ser Asp Gly Thr Phe Thr Ser Glu Leu Ser Arg Leu Arg Glu Gly
 1 5 10 15

Ala Arg Leu Gln Arg Leu Leu Gln Gly Leu Val
 20 25

<210> 356

<211> 120

<212> PRT

<213> Homo sapiens

<400> 356

Ser Ser Ser His Pro Ile Phe His Arg Gly Glu Phe Ser Val Cys Asp
 1 5 10 15

Ser Val Ser Val Trp Val Gly Asp Lys Thr Thr Ala Thr Asp Ile Lys
 20 25 30

Gly Lys Glu Val Met Val Leu Gly Glu Val Asn Ile Asn Asn Ser Val
 35 40 45

Phe Lys Gln Tyr Phe Phe Glu Thr Lys Cys Arg Asp Pro Asn Pro Val
 50 55 60

Asp Ser Gly Cys Arg Gly Ile Asp Ser Lys His Trp Asn Ser Tyr Cys
 65 70 75 80

Thr Thr Thr His Thr Phe Val Lys Ala Leu Thr Met Asp Gly Lys Gln
 85 90 95

Ala Ala Trp Arg Phe Ile Arg Ile Asp Thr Ala Cys Val Cys Val Leu
 100 105 110

Ser Arg Lys Ala Val Arg Arg Ala
 115 120

<210> 357

<211> 120

<212> PRT

<213> Homo sapiens

<400> 357

Ser Ser Ser His Pro Ile Phe His Arg Gly Glu Phe Ser Val Cys Asp
 1 5 10 15

Ser Val Ser Val Trp Val Gly Asp Lys Thr Thr Ala Thr Asp Ile Lys
 20 25 30

Gly Lys Glu Val Met Val Leu Gly Glu Val Asn Ile Asn Asn Ser Val
 35 40 45

Phe Lys Gln Tyr Phe Phe Glu Thr Lys Cys Arg Asp Pro Asn Pro Val

50 55 60
 Asp Ser Gly Cys Arg Gly Ile Asp Ser Lys His Trp Asn Ser Tyr Cys
 65 70 75 80
 Thr Thr Thr His Thr Phe Val Lys Ala Leu Thr Met Asp Gly Lys Gln
 85 90 95
 Ala Ala Trp Arg Phe Ile Arg Ile Asp Thr Ala Cys Val Cys Val Leu
 100 105 110
 Ser Arg Lys Ala Val Arg Arg Ala
 115 120

<210> 358
 <211> 120
 <212> PRT
 <213> Homo sapiens

<400> 358
 Ser Ser Ser His Pro Ile Phe His Arg Gly Glu Phe Ser Val Cys Asp
 1 5 10 15
 Ser Val Ser Val Trp Val Gly Asp Lys Thr Thr Ala Thr Asp Ile Lys
 20 25 30
 Gly Lys Glu Val Met Val Leu Gly Glu Val Asn Ile Asn Asn Ser Val
 35 40 45
 Phe Lys Gln Tyr Phe Phe Glu Thr Lys Cys Arg Asp Pro Asn Pro Val
 50 55 60
 Asp Ser Gly Cys Arg Gly Ile Asp Ser Lys His Trp Asn Ser Tyr Cys
 65 70 75 80
 Thr Thr Thr His Thr Phe Val Lys Ala Leu Thr Met Asp Gly Lys Gln
 85 90 95
 Ala Ala Trp Arg Phe Ile Arg Ile Asp Thr Ala Cys Val Cys Val Leu
 100 105 110
 Ser Arg Lys Ala Val Arg Arg Ala
 115 120

<210> 359
 <211> 120
 <212> PRT
 <213> Homo sapiens

<400> 359
 Ser Ser Ser His Pro Ile Phe His Arg Gly Glu Phe Ser Val Cys Asp
 1 5 10 15
 Ser Val Ser Val Trp Val Gly Asp Lys Thr Thr Ala Thr Asp Ile Lys
 20 25 30

Gly Lys Glu Val Met Val Leu Gly Glu Val Asn Ile Asn Asn Ser Val
 35 40 45
 Phe Lys Gln Tyr Phe Phe Glu Thr Lys Cys Arg Asp Pro Asn Pro Val
 50 55 60
 Asp Ser Gly Cys Arg Gly Ile Asp Ser Lys His Trp Asn Ser Tyr Cys
 65 70 75 80
 Thr Thr Thr His Thr Phe Val Lys Ala Leu Thr Met Asp Gly Lys Gln
 85 90 95
 Ala Ala Trp Arg Phe Ile Arg Ile Asp Thr Ala Cys Val Cys Val Leu
 100 105 110
 Ser Arg Lys Ala Val Arg Arg Ala
 115 120

<210> 360
 <211> 69
 <212> PRT
 <213> Homo sapiens

<400> 360
 Arg Ser Leu Gln Asp Thr Glu Glu Lys Ser Arg Ser Phe Ser Ala Ser
 1 5 10 15
 Gln Ala Asp Pro Leu Ser Asp Pro Asp Gln Met Asn Glu Asp Lys Arg
 20 25 30
 His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
 35 40 45
 Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
 50 55 60
 Arg Asn Asn Ile Ala
 65

<210> 361
 <211> 69
 <212> PRT
 <213> Homo sapiens

<400> 361
 Arg Ser Leu Gln Asp Thr Glu Glu Lys Ser Arg Ser Phe Ser Ala Ser
 1 5 10 15
 Gln Ala Asp Pro Leu Ser Asp Pro Asp Gln Met Asn Glu Asp Lys Arg
 20 25 30
 His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
 35 40 45
 Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn

50

55

60

Arg Asn Asn Ile Ala
65

<210> 362

<211> 37

<212> PRT

<213> Homo sapiens

<400> 362

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 363

<211> 37

<212> PRT

<213> Homo sapiens

<400> 363

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 364

<211> 27

<212> PRT

<213> Homo sapiens

<400> 364

His Ala Asp Gly Val Phe Thr Ser Asp Phe Ser Lys Leu Leu Gly Gln
1 5 10 15

Leu Ser Ala Lys Lys Tyr Leu Glu Ser Leu Met
20 25

<210> 365

<211> 27

<212> PRT

<213> Homo sapiens

<400> 365

His Ala Asp Gly Val Phe Thr Ser Asp Phe Ser Lys Leu Leu Gly Gln
1 5 10 15

Leu Ser Ala Lys Lys Tyr Leu Glu Ser Leu Met
 20 25

<210> 366
 <211> 27
 <212> PRT
 <213> Homo sapiens

<220>
 <221> MISC_FEATURE
 <222> (1)
 <223> Xaa equals thiopropionic acid (Tpa)

<220>
 <221> MISC_FEATURE
 <222> (23)
 <223> Xaa equals biphenylalanine (Bip)

<400> 366
 Xaa Asn Leu His Phe Cys Gln Leu Arg Cys Lys Ser Leu Gly Leu Leu
 1 5 10 15

Gly Lys Cys Ala Gly Ser Xaa Cys Ala Cys Val
 20 25

<210> 367
 <211> 27
 <212> PRT
 <213> Homo sapiens

<220>
 <221> MISC_FEATURE
 <222> (1)
 <223> Xaa equals thiopropionic acid (Tpa)

<220>
 <221> MISC_FEATURE
 <222> (23)
 <223> Xaa equals biphenylalanine (Bip)

<400> 367
 Xaa Asn Leu His Phe Cys Gln Leu Arg Cys Lys Ser Leu Gly Leu Leu
 1 5 10 15

Gly Lys Cys Ala Gly Ser Xaa Cys Ala Cys Val
 20 25

<210> 368
 <211> 52
 <212> PRT
 <213> Homo sapiens

<400> 368
 Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Ser Pro Lys Met Val Gln
 20 25 30
 Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser
 35 40 45
 Gly Leu Gly Cys
 50

<210> 369
 <211> 28
 <212> PRT
 <213> Homo sapiens

<400> 369
 Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15
 Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val
 20 25

<210> 370
 <211> 32
 <212> PRT
 <213> Homo sapiens

<400> 370
 Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15
 Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
 20 25 30

<210> 371
 <211> 27
 <212> PRT
 <213> Homo sapiens

<400> 371
 Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
 1 5 10 15
 Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys
 20 25

<210> 372

<211> 20
<212> DNA
<213> Homo sapiens

<400> 372
gagttcttcc catacaaact 20

<210> 373
<211> 21
<212> DNA
<213> Homo sapiens

<400> 373
catgatcttc aaatggacac t 21

<210> 374
<211> 20
<212> DNA
<213> Homo sapiens

<400> 374
gagttcttcc catacaaact 20

<210> 375
<211> 21
<212> DNA
<213> Homo sapiens

<400> 375
catgatcttc aaatggacac t 21

<210> 376
<211> 23
<212> DNA
<213> Homo sapiens

<400> 376
gcacacgctg gaccttacca ccc 23

<210> 377
<211> 30
<212> DNA
<213> Homo sapiens

<400> 377
attccatcga tgagcaacct cactcttgtg 30

<210> 378
<211> 21
<212> DNA
<213> Homo sapiens

<400> 378
aggagcgtcg acaaagaag c 21

<210> 379
<211> 19

<212> DNA
<213> Homo sapiens

<400> 379
cgcgcatcga tgagcaacc 19

<210> 380
<211> 41
<212> DNA
<213> Homo sapiens

<400> 380
gccgctgcct taggcttagc caccatgggtg agcaaggcg a 41

<210> 381
<211> 33
<212> DNA
<213> Homo sapiens

<400> 381
ctgcatccta aggttacttg tacagctcgt cca 33

<210> 382
<211> 20
<212> DNA
<213> Homo sapiens

<400> 382
catacaaaact taagagtcca 20

<210> 383
<211> 56
<212> DNA
<213> Homo sapiens

<400> 383
ctttaaatcg atgagcaacc tcactcttgt gtgcatcagc gttagccaaa gaagca 56

<210> 384
<211> 20
<212> DNA
<213> Homo sapiens

<400> 384
catacaaaact taagagtcca 20

<210> 385
<211> 56
<212> DNA
<213> Homo sapiens

<400> 385
ctttaaatcg atgagcaacc tcactcttgt gtgcatctgc cgatattttg gctgca 56

<210> 386
<211> 20
<212> DNA

<213> Homo sapiens

<400> 386

catacaaaact taagagtcca

20

<210> 387

<211> 56

<212> DNA

<213> Homo sapiens

<400> 387

ctttaaatcg atgagcaacc tcactcttgt gtgcatctct cttatccaaa gaacct

56

<210> 388

<211> 41

<212> DNA

<213> Homo sapiens

<400> 388

gccgctgcct taggcttagc caccatgggtg agcaagggcg a

41

<210> 389

<211> 33

<212> DNA

<213> Homo sapiens

<400> 389

ctgcatccta aggttacttg tacagctcgt cca

33

<210> 390

<211> 74

<212> DNA

<213> Homo sapiens

<400> 390

aattcattgc ttggttggtt aagggtagag atgcacacaa gaggtaggat gcacacaaga
gtgaggttgc tcat

60

74

<210> 391

<211> 72

<212> DNA

<213> Homo sapiens

<400> 391

cgatgagcaa cctcactctt gtgtgcatcc tcactcttgt gtgcatctct acccttaacc
aaccaagcaa tg

60

72

<210> 392

<211> 98

<212> DNA

<213> Homo sapiens

<400> 392

aattcattgc ttggttggtt aagggtagag atgcacacaa gaggtaggtt gctcatcgat
ttaagattt ggatgcacac aagagtgagg ttgctcat

60

98

<210> 393

<211> 96
 <212> DNA
 <213> Homo sapiens

<400> 393
 cgatgagcaa cctcactctt gtgtgcatcc aaatctttaa atcgatgagc aacctcactc 60
 ttgtgtgcat ctctaccctt aaccaaccaa gcaatg 96

<210> 394
 <211> 48
 <212> DNA
 <213> Homo sapiens

<400> 394
 ccgccgctcg aggggtgtgt ttcgtcgaag cccaagatg gtgcaagg 48

<210> 395
 <211> 57
 <212> DNA
 <213> Homo sapiens

<400> 395
 agtcccatcg atgagcaacc tcactcttgt gtgcatcatg ccgcctcagc actttgc 57

<210> 396
 <211> 95
 <212> DNA
 <213> Homo sapiens

<400> 396
 aattcattgc ttggttggtt aagggtagag atgcacacaa gaggtagggtt gctcatcgat 60
 ttaaatgaga tgcacacaag agtgagggtg ctcat 95

<210> 397
 <211> 93
 <212> DNA
 <213> Homo sapiens

<400> 397
 cgatgagcaa cctcactctt gtgtgcatca tctttaaatc gatgagcaac ctcactcttg 60
 tgtgcatctc tacccttaac caaccaagca atg 93

<210> 398
 <211> 48
 <212> DNA
 <213> Homo sapiens

<400> 398
 ccgccgctcg aggggtgtgt ttcgtcgaag cccaagatg gtgcaagg 48

<210> 399
 <211> 57
 <212> DNA
 <213> Homo sapiens

<400> 399
 agtcccatcg atgagcaacc tcactcttgt gtgcatcatg ccgcctcagc actttgc 57

<210> 400
 <211> 38
 <212> DNA
 <213> Homo sapiens

 <400> 400
 aggagcgtcg acaaaagaag cctgcggaga tccagctg 38

 <210> 401
 <211> 56
 <212> DNA
 <213> Homo sapiens

 <400> 401
 gctgtaacag cttccggtac gatgcacaca agagtgaggt tgctcatcga tgcgcg 56

 <210> 402
 <211> 77
 <212> DNA
 <213> Homo sapiens

 <400> 402
 aattcattgc ttggttggtt aagggtagag atgcacacaa gagtgaggtt gatgcacaca 60
 agagtgaggt tgctcat 77

 <210> 403
 <211> 75
 <212> DNA
 <213> Homo sapiens

 <400> 403
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 accaaccaag caatg 75

 <210> 404
 <211> 92
 <212> DNA
 <213> Homo sapiens

 <400> 404
 aattcattgc ttggttggtt aagggtagag atgcacacaa gagtgaggtt gctcatcgat 60
 ttaaagatgc acacaagagt gaggttgctc at 92

 <210> 405
 <211> 90
 <212> DNA
 <213> Homo sapiens

 <400> 405
 cgatgagcaa cctcactctt gtgtgcatct ttaaactgat gagcaacctc actcttgtgt 60
 gcattcttac ccttaacca ccaagcaatg 90

 <210> 406
 <211> 18
 <212> DNA
 <213> Homo sapiens

<400> 406
gcaatcaaac ccgaggct 18

<210> 407
<211> 21
<212> DNA
<213> Homo sapiens

<400> 407
ctttaaatcg atgagcaacc t 21

<210> 408
<211> 37
<212> DNA
<213> Homo sapiens

<400> 408
aggagcgtcg acaaaagaag cccaagatg gtgcaag 37

<210> 409
<211> 59
<212> DNA
<213> Homo sapiens

<400> 409
cgcgcatcga tgagcaacct cactcttggtg tgcattccagc actttgcagc ccaggccac 59

<210> 410
<211> 23
<212> DNA
<213> Homo sapiens

<400> 410
gcaagcccca agatggtgca agg 23

<210> 411
<211> 59
<212> DNA
<213> Homo sapiens

<400> 411
cgcgcatcga tgagcaacct cactcttggtg tgcattccagc actttgcagc ccaggccac 59

<210> 412
<211> 48
<212> DNA
<213> Homo sapiens

<400> 412
ccgcgctcg aggggtgtgt ttcgtcgaag cccaagatg gtgcaagg 48

<210> 413
<211> 57
<212> DNA
<213> Homo sapiens

<400> 413
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<210> 414
<211> 48
<212> DNA
<213> Homo sapiens

<400> 414
ccgccgctcg aggggtgtgt ttcgtcgaag cccaagatg gtgcaagg 48

<210> 415
<211> 57
<212> DNA
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<400> 415
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<210> 416
<211> 23
<212> DNA
<213> Homo sapiens

<400> 416
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<210> 417
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<212> DNA
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<210> 418
<211> 23
<212> DNA
<213> Homo sapiens

<400> 418
gcaagcccca agatggtgca agg 23

<210> 419
<211> 58
<212> DNA
<213> Homo sapiens

<400> 419
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<210> 420
<211> 23
<212> DNA
<213> Homo sapiens

<400> 420

gcaagcccca agatggtgca agg 23

<210> 421
 <211> 61
 <212> DNA
 <213> Homo sapiens

<400> 421
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 g 61

<210> 422
 <211> 37
 <212> DNA
 <213> Homo sapiens

<400> 422
 aggagcgtcg acaaaagaag cccaagatg gtgcaag 37

<210> 423
 <211> 56
 <212> DNA
 <213> Homo sapiens

<400> 423
 cgcgcatcga tgagcaacct cactcttggtg tgcattccact ttgcagccca ggccac 56
 tggagg

<210> 424
 <211> 37
 <212> DNA
 <213> Homo sapiens

<400> 424
 aggagcgtcg acaaaagaag cccaagatg gtgcaag 37

<210> 425
 <211> 56
 <212> DNA
 <213> Homo sapiens

<400> 425
 cgcgcatcga tgagcaacct cactcttggtg tgcattccact ttgcagccca ggccac 56

<210> 426
 <211> 103
 <212> DNA
 <213> Homo sapiens

<400> 426
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 tgctgtggcc catggtgtgg gccagcccca agatggtgca agg 103

<210> 427
 <211> 57
 <212> DNA
 <213> Homo sapiens

<400> 427
 agtcccatcg atgagcaacc tcactcttgt gtgcatcatg ccgcctcagc actttgc 57

<210> 428
 <211> 37
 <212> DNA
 <213> Homo sapiens

<400> 428
 aggagcgtcg acaaaagaag cccaagatg gtgcaag 37

<210> 429
 <211> 53
 <212> DNA
 <213> Homo sapiens

<400> 429
 cgcgcatcga tgagcaacct cactcttgtg tgcattcttg cagcccaggc cac 53

<210> 430
 <211> 774
 <212> PRT
 <213> Homo sapiens

<400> 430
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Cys Asp Leu Pro Gln Thr His Ser
 20 25 30
 Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile
 35 40 45
 Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln
 50 55 60
 Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu
 65 70 75 80
 His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser
 85 90 95
 Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu
 100 105 110
 Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly
 115 120 125
 Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg
 130 135 140
 Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser
 145 150 155 160
 Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser

165	170	175
Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu Asp Ala His		
180	185	190
Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe		
195	200	205
Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro		
210	215	220
Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys		
225	230	235
Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His		
245	250	255
Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr		
260	265	270
Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn		
275	280	285
Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu		
290	295	300
Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu		
305	310	315
Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro		
325	330	335
Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala		
340	345	350
Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu		
355	360	365
Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys		
370	375	380
Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe		
385	390	395
Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu		
405	410	415
Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr		
420	425	430
Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp		
435	440	445
Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu		
450	455	460
Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala		

465 470 475 480
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 485 490 495
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 500 505 510
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 515 520 525
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 530 535 540
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 545 550 555 560
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 565 570 575
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 580 585 590
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 595 600 605
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 610 615 620
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 625 630 635 640
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 645 650 655
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 660 665 670
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 675 680 685
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 690 695 700
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 705 710 715 720
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 725 730 735
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 740 745 750
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 755 760 765
 Gln Ala Ala Leu Gly Leu

770

<210> 431
 <211> 498
 <212> DNA
 <213> Homo sapiens

<400> 431
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 atgaggagaa tctctctttt ctctgcttg aaggacagac atgactttgg atttccccag 120
 gaggagtttg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
 cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttggga tgagaccctc 240
 ctagacaaat tctacactga actctaccag cagctgaatg acctggaagc ctgtgtgata 300
 cagggggtgg ggggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg 360
 aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg 420
 gaggttgtca gagcagaaat catgagatct ttttctttgt caacaaactt gcaagaaagt 480
 ttaagaagta aggaataa 498

<210> 432
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 432
 Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
 100 105 110
 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125
 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
 145 150 155 160
 Leu Arg Ser Lys Glu
 165

<210> 433

<211> 41

<212> DNA

<213> Homo sapiens

<400> 433

cgcgcgctgc gacaaaagat gtgatctgcc tcaaaccac a

41

<210> 434

<211> 59

<212> DNA

<213> Homo sapiens

<400> 434

gcgcgcatcg atgagcaacc tcactcttgt gtgcatcttc cttacttctt aaactttct

59

<210> 435

<211> 769

<212> PRT

<213> Homo sapiens

<400> 435

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
1 5 10 15Ile Ser Ala Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg
20 25 30Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys
35 40 45Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn
50 55 60Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln
65 70 75 80Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp
85 90 95Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn
100 105 110Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro
115 120 125Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg
130 135 140Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu
145 150 155 160Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu
165 170 175Gln Glu Ser Leu Arg Ser Lys Glu Asp Ala His Lys Ser Glu Val Ala
180 185 190

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 195 200 205
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 210 215 220
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 225 230 235 240
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 245 250 255
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 260 265 270
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 275 280 285
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 290 295 300
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 305 310 315 320
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 325 330 335
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 340 345 350
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 355 360 365
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 370 375 380
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 385 390 395 400
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 405 410 415
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 420 425 430
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 435 440 445
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 450 455 460
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 465 470 475 480
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 485 490 495

Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 500 505 510
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 515 520 525
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 530 535 540
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 545 550 555 560
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 565 570 575
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 580 585 590
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 595 600 605
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 610 615 620
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 625 630 635 640
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 645 650 655
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 660 665 670
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 675 680 685
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 690 695 700
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 705 710 715 720
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 725 730 735
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 740 745 750
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 755 760 765
 Leu
 <210> 436
 <211> 495
 <212> DNA

<213> Homo sapiens

<400> 436

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atgaggagaa tctctctttt ctctgcttg aaggacagac atgacttttg atttcccag    120
gaggagtgtg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgatc    180
cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttgga tgagaccctc    240
ctagacaaat tctacactga actctaccag cagctgaatg acctggaagc ctgtgtgata    300
cagggggtgg ggggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg    360
aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg    420
gaggttgtca gagcagaaat catgagatct ttttcttgt caacaaactt gcaagaaagt    480
ttaagaagta aggaa                                         495

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<210> 437

<211> 165

<212> PRT

<213> Homo sapiens

<400> 437

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1              5              10              15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
      20              25              30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
      35              40              45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
      50              55              60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
      65              70              75              80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
      85              90              95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
      100              105              110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
      115              120              125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
      130              135              140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
      145              150              155              160

Leu Arg Ser Lys Glu
      165

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<210> 438

<211> 27

<212> DNA

<213> Homo sapiens

<400> 438

g t t a g c a g a g t a g c a g g g c t t t c g g c t

27

<210> 439

<211> 59

<212> DNA

<213> Homo sapiens

<400> 439

g c g c g c a t c g a t g a g c a a c c t c a c t c t t g t g t g c a t c t t c c t t a c t t c t t a a a c t t t c t

59

<210> 440

<211> 835

<212> PRT

<213> Homo sapiens

<400> 440

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20 25 30Ile Pro Ala Glu Ala Val Ile Gly Tyr Ser Asp Leu Glu Gly Asp Phe
35 40 45Asp Val Ala Val Leu Pro Phe Ser Asn Ser Thr Asn Asn Gly Leu Leu
50 55 60Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys Glu Glu Gly Val
65 70 75 80Ser Leu Asp Lys Arg Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser
85 90 95Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe
100 105 110Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe
115 120 125Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met
130 135 140Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala
145 150 155 160Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln
165 170 175Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu
180 185 190Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe
195 200 205

Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala

210	215	220
Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr		
225	230	235 240
Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu Asp Ala His Lys Ser Glu		
	245	250 255
Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu		
	260	265 270
Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp		
	275	280 285
His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val		
	290	295 300
Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe		
305	310	315 320
Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu		
	325	330 335
Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe		
	340	345 350
Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro		
	355	360 365
Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe		
	370	375 380
Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr		
385	390	395 400
Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr		
	405	410 415
Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu		
	420	425 430
Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu		
	435	440 445
Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp		
	450	455 460
Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu		
465	470	475 480
Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys		
	485	490 495
His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys		
	500	505 510
Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys		

515	520	525
Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu 530 535 540		
Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val 545 550 555 560		
Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe 565 570 575		
Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser 580 585 590		
Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu 595 600 605		
Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe 610 615 620		
Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln 625 630 635 640		
Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala 645 650 655		
Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr 660 665 670		
Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys 675 680 685		
Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser 690 695 700		
Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser 705 710 715 720		
Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro 725 730 735		
Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe 740 745 750		
Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu 755 760 765		
Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys 770 775 780		
His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp 785 790 795 800		
Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr 805 810 815		
Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala		

820

825

830

Leu Gly Leu
835

<210> 441

<211> 495

<212> DNA

<213> Homo sapiens

<400> 441

tgtgatctgc	ctcaaacc	cagcctgggt	tctagaagga	ccttgatgct	cctggcacag	60
atgaggagaa	tctctctttt	ctcctgcttg	aaggacagac	atgactttgg	atttccccag	120
gaggagtttg	gcaaccagtt	ccaaaaggct	gaaacccatcc	ctgtcctcca	tgagatgât	180
cagcagatct	tcaatctctt	cagcacaaag	gactcatctg	ctgcttgga	tgagaccctc	240
ctagacaaat	tctacactga	actctaccag	cagctgaatg	acctggaagc	ctgtgtgata	300
caggggggtgg	gggtgacaga	gactcccctg	atgaaggagg	actccattct	ggctgtgagg	360
aaatacttcc	aaagaatcac	tctctatctg	aaagagaaga	aatacagccc	ttgtgcctgg	420
gaggttgta	gagcagaaat	catgagatct	ttttctttgt	caacaaactt	gcaagaaagt	480
ttaagaagta	aggaa					495

<210> 442

<211> 165

<212> PRT

<213> Homo sapiens

<400> 442

Cys	Asp	Leu	Pro	Gln	Thr	His	Ser	Leu	Gly	Ser	Arg	Arg	Thr	Leu	Met
1					5				10					15	
Leu	Leu	Ala	Gln	Met	Arg	Arg	Ile	Ser	Leu	Phe	Ser	Cys	Leu	Lys	Asp
		20						25					30		
Arg	His	Asp	Phe	Gly	Phe	Pro	Gln	Glu	Glu	Phe	Gly	Asn	Gln	Phe	Gln
		35					40					45			
Lys	Ala	Glu	Thr	Ile	Pro	Val	Leu	His	Glu	Met	Ile	Gln	Gln	Ile	Phe
	50					55					60				
Asn	Leu	Phe	Ser	Thr	Lys	Asp	Ser	Ser	Ala	Ala	Trp	Asp	Glu	Thr	Leu
	65				70					75					80
Leu	Asp	Lys	Phe	Tyr	Thr	Glu	Leu	Tyr	Gln	Gln	Leu	Asn	Asp	Leu	Glu
		85						90					95		
Ala	Cys	Val	Ile	Gln	Gly	Val	Gly	Val	Thr	Glu	Thr	Pro	Leu	Met	Lys
		100					105						110		
Glu	Asp	Ser	Ile	Leu	Ala	Val	Arg	Lys	Tyr	Phe	Gln	Arg	Ile	Thr	Leu
	115						120					125			
Tyr	Leu	Lys	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val	Arg
	130					135						140			
Ala	Glu	Ile	Met	Arg	Ser	Phe	Ser	Leu	Ser	Thr	Asn	Leu	Gln	Glu	Ser
	145				150					155				160	

Leu Arg Ser Lys Glu
165

<210> 443

<211> 41

<212> DNA

<213> Homo sapiens

<400> 443

cgcgcgctgc gacaaaagat gtgatctgcc tcaaaccac a

41

<210> 444

<211> 59

<212> DNA

<213> Homo sapiens

<400> 444

gcgcgcctcg atgagcaacc tcaactctgt gtgcattctt cttacttctt aaactttct

59

<210> 445

<211> 774

<212> PRT

<213> Homo sapiens

<400> 445

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Gly Val Phe Arg Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480

Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu
 610 615 620
 Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys
 625 630 635 640
 Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe
 645 650 655
 Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
 660 665 670
 Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
 675 680 685
 Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
 690 695 700
 Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
 705 710 715 720
 Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
 725 730 735
 Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
 740 745 750
 Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu
 755 760 765
 Ser Leu Arg Ser Lys Glu
 770

<210> 446
 <211> 495
 <212> DNA
 <213> Homo sapiens

<400> 446
 tgtgatctgc ctcaaaccga cagcctgggt tctagaagga ccttgatgct cctggcacag 60
 atgaggagaa tctctctttt ctctctgttg aaggacagac atgacttttg atttccccag 120
 gaggagtgtg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgatc 180
 cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttggga tgagaccctc 240
 ctagacaaat tctacactga actctaccag cagctgaatg acctggaagc ctgtgtgata 300
 caggggtgg gggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg 360
 aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg 420
 gaggtgtgca gagcagaaat catgagatct ttttctttgt caacaaactt gcaagaaagt 480
 ttaagaagta aggaa 495

<210> 447
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 447
 Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
 100 105 110
 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125
 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
 145 150 155 160
 Leu Arg Ser Lys Glu
 165

<210> 448

<211> 38
 <212> DNA
 <213> Homo sapiens

<400> 448
 caagctgcct taggcttatg tgatctgcct caaaccca

38

<210> 449
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 449
 gaattcggcg cgccttatcc cttacttctt aaactttct

39

<210> 450
 <211> 773
 <212> PRT
 <213> Homo sapiens

<400> 450
 Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys
 1 5 10 15
 Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu
 20 25 30
 Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser
 35 40 45
 Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
 50 55 60
 Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His
 65 70 75 80
 Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser
 85 90 95
 Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr
 100 105 110
 Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val
 115 120 125
 Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys
 130 135 140
 Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro
 145 150 155 160
 Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu
 165 170 175
 Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu Asp Ala His Lys
 180 185 190

Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys
 195 200 205
 Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe
 210 215 220
 Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr
 225 230 235 240
 Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr
 245 250 255
 Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr
 260 265 270
 Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu
 275 280 285
 Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val
 290 295 300
 Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu
 305 310 315 320
 Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr
 325 330 335
 Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala
 340 345 350
 Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro
 355 360 365
 Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln
 370 375 380
 Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys
 385 390 395 400
 Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe
 405 410 415
 Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu
 420 425 430
 Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu
 435 440 445
 Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys
 450 455 460
 Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu
 465 470 475 480
 Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp
 485 490 495

Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp
 500 505 510
 Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp
 515 520 525
 Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr
 530 535 540
 Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys
 545 550 555 560
 Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile
 565 570 575
 Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln
 580 585 590
 Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr
 595 600 605
 Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys
 610 615 620
 Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr
 625 630 635 640
 Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro
 645 650 655
 Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg
 660 665 670
 Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys
 675 680 685
 Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu
 690 695 700
 Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu
 705 710 715 720
 Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met
 725 730 735
 Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys
 740 745 750
 Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln
 755 760 765
 Ala Ala Leu Gly Leu
 770

<210> 451

<211> 495

<212> DNA

<213> Homo sapiens

<400> 451

tgtgatctgc	ctcaaacc	cagcctgggt	tctagaagga	ccttgatgct	cctggcacag	60
atgaggagaa	tctctctttt	ctcctgcttg	aaggacagac	atgactttgg	atttccccag	120
gaggagtttg	gcaaccagtt	ccaaaaggct	gaaaccatcc	ctgtcctcca	tgagatgatc	180
cagcagatct	tcaatctctt	cagcacaaag	gactcatctg	ctgcttgga	tgagaccctc	240
ctagacaaat	tctacactga	actctaccag	cagctgaatg	acctggaagc	ctgtgtgata	300
caggggggtgg	gggtgacaga	gactcccctg	atgaaggagg	actccattct	ggctgtgagg	360
aaatacttcc	aaagaatcac	tctctatctg	aaagagaaga	aatacagccc	ttgtgcctgg	420
gaggttgtca	gagcagaaat	catgagatct	ttttctttgt	caacaaactt	gcaagaaagt	480
ttagaagta	aggaa					495

<210> 452

<211> 165

<212> PRT

<213> Homo sapiens

<400> 452

Cys	Asp	Leu	Pro	Gln	Thr	His	Ser	Leu	Gly	Ser	Arg	Arg	Thr	Leu	Met
1				5					10					15	
Leu	Leu	Ala	Gln	Met	Arg	Arg	Ile	Ser	Leu	Phe	Ser	Cys	Leu	Lys	Asp
		20					25					30			
Arg	His	Asp	Phe	Gly	Phe	Pro	Gln	Glu	Glu	Phe	Gly	Asn	Gln	Phe	Gln
	35					40					45				
Lys	Ala	Glu	Thr	Ile	Pro	Val	Leu	His	Glu	Met	Ile	Gln	Gln	Ile	Phe
	50				55						60				
Asn	Leu	Phe	Ser	Thr	Lys	Asp	Ser	Ser	Ala	Ala	Trp	Asp	Glu	Thr	Leu
65					70				75					80	
Leu	Asp	Lys	Phe	Tyr	Thr	Glu	Leu	Tyr	Gln	Gln	Leu	Asn	Asp	Leu	Glu
		85						90						95	
Ala	Cys	Val	Ile	Gln	Gly	Val	Gly	Val	Thr	Glu	Thr	Pro	Leu	Met	Lys
		100					105						110		
Glu	Asp	Ser	Ile	Leu	Ala	Val	Arg	Lys	Tyr	Phe	Gln	Arg	Ile	Thr	Leu
	115					120					125				
Tyr	Leu	Lys	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val	Arg
	130					135					140				
Ala	Glu	Ile	Met	Arg	Ser	Phe	Ser	Leu	Ser	Thr	Asn	Leu	Gln	Glu	Ser
145					150					155				160	
Leu	Arg	Ser	Lys	Glu											
					165										

<210> 453

<211> 107

<212> DNA

<213> Homo sapiens

<400> 453
 gcgcgcggat ccgccaccat ggccttgacc tttgctttac tgggtggccct cctggtgctc 60
 agctgcaagt caagctgctc tgtgggctgt gatctgcctc aaaccca 107

<210> 454
 <211> 59
 <212> DNA
 <213> Homo sapiens

<400> 454
 gcgcgcatcg atgagcaacc tcactcttgt gtgcatcttc cttacttctt aaactttct 59

<210> 455
 <211> 769
 <212> PRT
 <213> Homo sapiens

<400> 455
 Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
 1 5 10 15
 Ile Ser Ala Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg
 20 25 30
 Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys
 35 40 45
 Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn
 50 55 60
 Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln
 65 70 75 80
 Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp
 85 90 95
 Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn
 100 105 110
 Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro
 115 120 125
 Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg
 130 135 140
 Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu
 145 150 155 160
 Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu
 165 170 175
 Gln Glu Ser Leu Arg Ser Lys Glu Asp Ala His Lys Ser Glu Val Ala
 180 185 190
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 195 200 205

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 210 215 220
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 225 230 235 240
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 245 250 255
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 260 265 270
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 275 280 285
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 290 295 300
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 305 310 315 320
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 325 330 335
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 340 345 350
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 355 360 365
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 370 375 380
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 385 390 395 400
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 405 410 415
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 420 425 430
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 435 440 445
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 450 455 460
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 465 470 475 480
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 485 490 495
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 500 505 510

Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 515 520 525
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 530 535 540
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 545 550 555 560
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 565 570 575
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 580 585 590
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 595 600 605
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 610 615 620
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 625 630 635 640
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 645 650 655
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 660 665 670
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 675 680 685
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 690 695 700
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 705 710 715 720
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 725 730 735
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 740 745 750
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 755 760 765

Leu

<210> 456

<211> 495

<212> DNA

<213> Homo sapiens

<400> 456

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tgtgatctgc ctcaaaccga cagcctgggt tctagaagga ccttgatgct cctggcacag    60
atgaggagaa tctctctttt ctcctgcttg aaggacagac atgacttttg atttccccag    120
gaggagtgtg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgatc    180
cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttgga tgagaccctc    240
ctagacaaat tctacactga actctaccag cagctgaatg acctggaagc ctgtgtgata    300
caggggggtg ggggtgacaga gactccccctg atgaaggagg actccattct ggctgtgagg    360
aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg    420
gaggttgtca gagcagaaat catgagatct ttttctttgt caacaaactt gcaagaaagt    480
ttaagaagta aggaa                                         495

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<210> 457

<211> 165

<212> PRT

<213> Homo sapiens

<400> 457

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
  1          5          10          15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
          20          25          30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
          35          40          45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
          50          55          60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
          65          70          75          80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
          85          90          95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
          100          105          110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
          115          120          125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
          130          135          140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
          145          150          155          160

Leu Arg Ser Lys Glu
          165

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<210> 458

<211> 25

<212> DNA

<213> Homo sapiens

<400> 458

gcatgtgatc tgcctcaaac ccaca

25

<210> 459

<211> 59

<212> DNA

<213> Homo sapiens

<400> 459

gcgcgcacgc atgagcaacc tcaactctgt gtgcaccttc cttacttctt aaactttct 59

<210> 460

<211> 774

<212> PRT

<213> Homo sapiens

<400> 460

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
180 185 190Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
195 200 205Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
210 215 220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525

Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu
 610 615 620
 Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys
 625 630 635 640
 Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe
 645 650 655
 Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
 660 665 670
 Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
 675 680 685
 Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
 690 695 700
 Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
 705 710 715 720
 Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
 725 730 735
 Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
 740 745 750
 Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu
 755 760 765
 Ser Leu Arg Ser Lys Glu
 770

<210> 461

<211> 495

<212> DNA

<213> Homo sapiens

<400> 461

tgtgatctgc ctcaaaccaca cagcctgggt tctagaagga ccttgatgct cctggcacag 60
 atgaggagaa tctctctttt ctctgcttg aaggacagac atgactttgg atttccccag 120

gaggagtttg gcaaccagtt ccaaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
 cagcagatct tcaatctctt cagcacaaag gactcatctg ctgcttggga tgagaccctc 240
 ctagacaaaat tctacactga actctaccag cagctgaatg acctggaagc ctgtgtgata 300
 caggggggtgg ggggtgacaga gactcccctg atgaaggagg actccattct ggctgtgagg 360
 aaatacttcc aaagaatcac tctctatctg aaagagaaga aatacagccc ttgtgcctgg 420
 gaggttgatca gagcagaaat catgagatct ttttctttgt caacaaactt gcaagaaagt 480
 ttaagaagta aggaa 495

<210> 462

<211> 165

<212> PRT

<213> Homo sapiens

<400> 462

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
 100 105 110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
 145 150 155 160

Leu Arg Ser Lys Glu
 165

<210> 463

<211> 775

<212> PRT

<213> Homo sapiens

<400> 463

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Met Ser Tyr Asn Leu Leu Gly Phe
 20 25 30
 Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu
 35 40 45
 Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile
 50 55 60
 Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala
 65 70 75 80
 Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln
 85 90 95
 Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu
 100 105 110
 Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu
 115 120 125
 Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu
 130 135 140
 His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys
 145 150 155 160
 Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg
 165 170 175
 Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn Asp Ala
 180 185 190
 His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
 195 200 205
 Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
 210 215 220
 Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
 225 230 235 240
 Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu
 245 250 255
 His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
 260 265 270
 Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
 275 280 285
 Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
 290 295 300
 Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
 305 310 315 320

Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
 325 330 335
 Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
 340 345 350
 Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
 355 360 365
 Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
 370 375 380
 Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
 385 390 395 400
 Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala
 405 410 415
 Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His
 420 425 430
 Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
 435 440 445
 Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys
 450 455 460
 Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile
 465 470 475 480
 Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala
 485 490 495
 Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala
 500 505 510
 Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His
 515 520 525
 Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu
 530 535 540
 Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr
 545 550 555 560
 Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn
 565 570 575
 Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys
 580 585 590
 Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val
 595 600 605
 Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly
 610 615 620

Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu
 625 630 635 640
 Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys
 645 650 655
 Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val
 660 665 670
 Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val
 675 680 685
 Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys
 690 695 700
 Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val
 705 710 715 720
 Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala
 725 730 735
 Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp
 740 745 750
 Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
 755 760 765
 Ser Gln Ala Ala Leu Gly Leu
 770 775

<210> 464

<211> 501

<212> DNA

<213> Homo sapiens

<400> 464

atgagctaca	acttgcttgg	attcctacaa	agaagcagca	attttcagtg	tcagaagctc	60
ctgtggcaat	tgaatgggag	gcttgaatat	tgccctcaagg	acaggatgaa	ctttgacatc	120
cctgaggaga	ttaagcagct	gcagcagttc	cagaaggagg	acgccgcatt	gaccatctat	180
gagatgctcc	agaacatctt	tgctattttc	agacaagatt	catctagcac	tggtctggaat	240
gagactattg	ttgagaacct	cctggctaata	gtctatcatc	agataaacca	tctgaagaca	300
gtcctggaag	aaaaactgga	gaaagaagat	ttcaccaggg	gaaaactcat	gagcagtcgt	360
cacctgaaaa	gatattatgg	gaggattctg	cattacctga	aggccaagga	gtacagtcac	420
tgtgcctgga	ccatagtcag	agtggaaatc	ctaaggaact	tttacttcat	taacagactt	480
acaggttacc	tccgaaacta	a				501

<210> 465

<211> 166

<212> PRT

<213> Homo sapiens

<400> 465

Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe	Gln
1				5					10					15	
Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
	20							25						30	

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35 40 45
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50 55 60
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65 70 75 80
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85 90 95
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
 100 105 110
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
 115 120 125
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160
 Thr Gly Tyr Leu Arg Asn
 165

<210> 466
 <211> 40
 <212> DNA
 <213> Homo sapiens

<400> 466
 cgcgcgctgc gacaaaagaa tgagctacaa cttgcttgga

40

<210> 467
 <211> 55
 <212> DNA
 <213> Homo sapiens

<400> 467
 gcgcgcacgc atgagcaacc tcaactctgt gtgcacgtt tcggaggtaa cctgt

55

<210> 468
 <211> 775
 <212> PRT
 <213> Homo sapiens

<400> 468
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu

35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly

340										345										350																									
Met	Phe	Leu	Tyr	Glu	Tyr	Ala	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Val																														
355										360										365																									
Leu	Leu	Leu	Arg	Leu	Ala	Lys	Thr	Tyr	Glu	Thr	Thr	Leu	Glu	Lys	Cys																														
370										375										380																									
Cys	Ala	Ala	Ala	Asp	Pro	His	Glu	Cys	Tyr	Ala	Lys	Val	Phe	Asp	Glu																														
385										390										395																									
Phe	Lys	Pro	Leu	Val	Glu	Glu	Pro	Gln	Asn	Leu	Ile	Lys	Gln	Asn	Cys																														
405										410										415																									
Glu	Leu	Phe	Glu	Gln	Leu	Gly	Glu	Tyr	Lys	Phe	Gln	Asn	Ala	Leu	Leu																														
420										425										430																									
Val	Arg	Tyr	Thr	Lys	Lys	Val	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val																														
435										440										445																									
Glu	Val	Ser	Arg	Asn	Leu	Gly	Lys	Val	Gly	Ser	Lys	Cys	Cys	Lys	His																														
450										455										460																									
Pro	Glu	Ala	Lys	Arg	Met	Pro	Cys	Ala	Glu	Asp	Tyr	Leu	Ser	Val	Val																														
465										470										475																									
Leu	Asn	Gln	Leu	Cys	Val	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Asp	Arg																														
485										490										495																									
Val	Thr	Lys	Cys	Cys	Thr	Glu	Ser	Leu	Val	Asn	Arg	Arg	Pro	Cys	Phe																														
500										505										510																									
Ser	Ala	Leu	Glu	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Asn	Ala																														
515										520										525																									
Glu	Thr	Phe	Thr	Phe	His	Ala	Asp	Ile	Cys	Thr	Leu	Ser	Glu	Lys	Glu																														
530										535										540																									
Arg	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Val	Glu	Leu	Val	Lys	His	Lys																														
545										550										555																									
Pro	Lys	Ala	Thr	Lys	Glu	Gln	Leu	Lys	Ala	Val	Met	Asp	Asp	Phe	Ala																														
565										570										575																									
Ala	Phe	Val	Glu	Lys	Cys	Cys	Lys	Ala	Asp	Asp	Lys	Glu	Thr	Cys	Phe																														
580										585										590																									
Ala	Glu	Glu	Gly	Lys	Lys	Leu	Val	Ala	Ala	Ser	Gln	Ala	Ala	Leu	Gly																														
595										600										605																									
Leu	Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe																														
610										615										620																									
Gln	Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys																														
625										630										635																									
Leu	Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu																														

645 650 655
 Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu
 660 665 670
 Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp
 675 680 685
 Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile
 690 695 700
 Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe
 705 710 715 720
 Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly
 725 730 735
 Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp
 740 745 750
 Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg
 755 760 765
 Leu Thr Gly Tyr Leu Arg Asn
 770 775

<210> 469
 <211> 501
 <212> DNA
 <213> Homo sapiens

<400> 469
 atgagctaca acttgcttgg attcctacaa agaagcagca attttcagtg tcagaagctc 60
 ctgtggcaat tgaatgggag gcttgaatat tgcctcaagg acaggatgaa ctttgacatc 120
 cctgaggaga ttaagcagct gcagcagttc cagaaggagg acgccgcatt gaccatctat 180
 gagatgctcc agaacatctt tgctattttc agacaagatt catctagcac tggctggaat 240
 gagactattg ttgagaacct cctggctaata gtctatcatc agataaacca tctgaagaca 300
 gtcttggaag aaaaactgga gaaagaagat ttcaccaggg gaaaactcat gagcagtctg 360
 cacctgaaaa gatattatgg gaggattctg cattacctga aggccaagga gtacagtcac 420
 tgtgcctgga ccatagtcag agtggaaatc ctaaggaact tttacttcat taacagactt 480
 acaggttacc tccgaaacta a 501

<210> 470
 <211> 166
 <212> PRT
 <213> Homo sapiens

<400> 470
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1 5 10 15
 Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20 25 30
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln

35 40 45
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50 55 60
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65 70 75 80
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85 90 95
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
 100 105 110
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
 115 120 125
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160
 Thr Gly Tyr Leu Arg Asn
 165

<210> 471

<211> 772

<212> PRT

<213> Homo sapiens

<400> 471

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15
 Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
 20 25 30
 Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
 35 40 45
 Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
 50 55 60
 Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
 65 70 75 80
 Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
 85 90 95
 Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
 100 105 110
 Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
 115 120 125
 Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys

130	135	140
Arg Tyr Tyr Gly Arg 145	Ile Leu His Tyr 150	Leu Lys Ala Lys Glu Tyr Ser 155 160
His Cys Ala Trp Thr 165	Ile Val Arg Val 170	Glu Ile Leu Arg Asn Phe Tyr 175
Phe Ile Asn Arg Leu Thr 180	Gly Tyr Leu Arg 185	Asn Asp Ala His Lys Ser 190
Glu Val Ala His Arg Phe 195	Lys Asp Leu Gly Glu Glu 200 205	Asn Phe Lys Ala
Leu Val Leu Ile Ala Phe 210	Ala Gln Tyr Leu Gln Gln 215 220	Cys Pro Phe Glu
Asp His Val Lys Leu Val 225	Asn Glu Val Thr Glu Phe 230 235	Ala Lys Thr Cys 240
Val Ala Asp Glu Ser Ala 245	Glu Asn Cys Asp Lys Ser 250	Leu His Thr Leu 255
Phe Gly Asp Lys Leu Cys 260	Thr Val Ala Thr Leu Arg 265	Glu Thr Tyr Gly 270
Glu Met Ala Asp Cys Cys 275	Ala Lys Gln Glu Pro Glu 280 285	Arg Asn Glu Cys
Phe Leu Gln His Lys Asp 290	Asp Asn Pro Asn Leu Pro 295 300	Arg Leu Val Arg
Pro Glu Val Asp Val Met 305	Cys Thr Ala Phe His Asp 310 315	Asn Glu Glu Thr 320
Phe Leu Lys Lys Tyr Leu 325	Tyr Glu Ile Ala Arg Arg 330	His Pro Tyr Phe 335
Tyr Ala Pro Glu Leu Leu 340	Phe Phe Ala Lys Arg Tyr 345	Lys Ala Ala Phe 350
Thr Glu Cys Cys Gln Ala 355	Ala Asp Lys Ala Ala Cys 360 365	Leu Leu Pro Lys
Leu Asp Glu Leu Arg Asp 370	Glu Gly Lys Ala Ser Ser 375 380	Ala Lys Gln Arg
Leu Lys Cys Ala Ser Leu 385	Gln Lys Phe Gly Glu Arg 390 395	Ala Phe Lys Ala 400
Trp Ala Val Ala Arg Leu 405	Ser Gln Arg Phe Pro Lys 410	Ala Glu Phe Ala 415
Glu Val Ser Lys Leu Val 420	Thr Asp Leu Thr Lys Val 425	His Thr Glu Cys 430
Cys His Gly Asp Leu Leu 440	Glu Cys Ala Asp Asp Arg 450	Ala Asp Leu Ala

435 440 445
 Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu
 450 455 460
 Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val
 465 470 475 480
 Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe
 485 490 495
 Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val
 500 505 510
 Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr
 515 520 525
 Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu
 530 535 540
 Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val
 545 550 555 560
 Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys
 565 570 575
 Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn
 580 585 590
 Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro
 595 600 605
 Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys
 610 615 620
 Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu
 625 630 635 640
 Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val
 645 650 655
 Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg
 660 665 670
 Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu
 675 680 685
 Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser
 690 695 700
 Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val
 705 710 715 720
 Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp
 725 730 735
 Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu

740 745 750
 Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
 755 760 765
 Ala Leu Gly Leu
 770
 <210> 472
 <211> 561
 <212> DNA
 <213> Homo sapiens
 <400> 472
 atgaccaaca agtgtctcct ccaaattgct ctctgttgt gcttctccac tacagctctt 60
 tccatgagct acaacttgct tggattccta caaagaagca gcaattttca gtgtcagaag 120
 ctctgtggc aattgaatgg gaggttgaa tattgcctca aggacaggat gaactttgac 180
 atccctgagg agattaagca gctgcagcag ttccagaagg aggacgccgc attgaccatc 240
 tatgagatgc tccagaacat ctttgctatt ttcagacaag attcatctag cactggctgg 300
 aatgagacta ttgttgagaa cctcctggct aatgtctatc atcagataaa ccatctgaag 360
 acagtccctgg aagaaaaact ggagaaagaa gatttcacca ggggaaaact catgagcagt 420
 ctgcacctga aaagatatta tgggaggatt ctgcattacc tgaaggccaa ggagtacagt 480
 cactgtgcct ggaccatagt cagagtggaa atcctaagga acttttactt cattaacaga 540
 cttacagggtt acctccgaaa c 561
 <210> 473
 <211> 187
 <212> PRT
 <213> Homo sapiens
 <400> 473
 Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15
 Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
 20 25 30
 Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
 35 40 45
 Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
 50 55 60
 Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
 65 70 75 80
 Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
 85 90 95
 Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
 100 105 110
 Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
 115 120 125
 Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
 130 135 140

Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
145 150 155 160

His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
165 170 175

Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
180 185

<210> 474

<211> 106

<212> DNA

<213> Homo sapiens

<400> 474

gcgcggatcc gaattccgcc gccatgacca acaagtgtct cctccaaatt gctctcctgt 60
tgtgcttctc cactacagct ctttccatga gctacaactt gcttgg 106

<210> 475

<211> 55

<212> DNA

<213> Homo sapiens

<400> 475

gcgcgcatcg atgagcaacc tcactcttgt gtgcatcggt tcggaggtaa cctgt 55

<210> 476

<211> 775

<212> PRT

<213> Homo sapiens

<400> 476

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Gly Val Phe Arg Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430

Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe
 610 615 620
 Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys
 625 630 635 640
 Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu
 645 650 655
 Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu
 660 665 670
 Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp
 675 680 685
 Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile
 690 695 700
 Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe
 705 710 715 720
 Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly
 725 730 735

Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp
740 745 750

Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg
755 760 765

Leu Thr Gly Tyr Leu Arg Asn
770 775

<210> 477

<211> 498

<212> DNA

<213> Homo sapiens

<400> 477

atgagctaca acttgcttgg attcctacaa agaagcagca attttcagtgc tcagaagctc 60
ctgtggcaat tgaatgggag gcttgaatat tgcctcaagg acaggatgaa ctttgacatc 120
cctgaggaga ttaagcagct gcagcagttc cagaaggagg acgccgcatt gaccatctat 180
gagatgctcc agaacatctt tgctattttc agacaagatt catctagcac tggctggaat 240
gagactattg ttgagaacct cctggctaata gtctatcatc agataaacca tctgaagaca 300
gtcctggaag aaaaactgga gaaagaagat ttcaccaggg gaaaactcat gagcagctctg 360
cacctgaaaa gatattatgg gaggattctg cattacctga aggcccaagga gtacagtcac 420
tgtgcctgga ccatagtcag agtggaaatc ctaaggaact tttacttcat taacagactt 480
acaggttacc tccgaaac 498

<210> 478

<211> 166

<212> PRT

<213> Homo sapiens

<400> 478

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160

Thr Gly Tyr Leu Arg Asn
 165

<210> 479

<211> 772

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (240)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> MISC_FEATURE

<222> (270)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 479

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15

Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
 20 25 30

Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
 35 40 45

Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
 50 55 60

Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
 65 70 75 80

Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
 85 90 95

Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
 100 105 110

Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
 115 120 125

Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
 130 135 140

Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
 145 150 155 160

His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
 165 170 175

Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn Asp Ala His Lys Ser
 180 185 190
 Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala
 195 200 205
 Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu
 210 215 220
 Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Xaa
 225 230 235 240
 Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu
 245 250 255
 Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Xaa Tyr Gly
 260 265 270
 Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys
 275 280 285
 Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg
 290 295 300
 Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr
 305 310 315 320
 Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe
 325 330 335
 Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe
 340 345 350
 Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys
 355 360 365
 Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg
 370 375 380
 Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala
 385 390 395 400
 Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala
 405 410 415
 Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys
 420 425 430
 Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala
 435 440 445
 Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu
 450 455 460
 Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val
 465 470 475 480

Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe
 485 490 495
 Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val
 500 505 510
 Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr
 515 520 525
 Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu
 530 535 540
 Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val
 545 550 555 560
 Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys
 565 570 575
 Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn
 580 585 590
 Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro
 595 600 605
 Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys
 610 615 620
 Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu
 625 630 635 640
 Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val
 645 650 655
 Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg
 660 665 670
 Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu
 675 680 685
 Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser
 690 695 700
 Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val
 705 710 715 720
 Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp
 725 730 735
 Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu
 740 745 750
 Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
 755 760 765
 Ala Leu Gly Leu
 770

<210> 480
 <211> 561
 <212> DNA
 <213> Homo sapiens

<400> 480
 atgaccaaca agtgtctcct ccaaattgct ctctgttgt gcttctccac tacagctctt 60
 tccatgagct acaacttgct tggattccta caaagaagca gcaattttca gtgtcagaag 120
 ctctgtggc aattgaatgg gaggttgaa tattgcctca aggacaggat gaactttgac 180
 atccctgagg agattaagca gctgcagcag ttccagaagg aggacgccgc attgaccatc 240
 tatgagatgc tccagaacat ctttgctatt ttcagacaag attcatctag cactggctgg 300
 aatgagacta ttgttgagaa cctcctggct aatgtctatc atcagataaa ccatctgaag 360
 acagtcctgg aagaaaaact ggagaaaagaa gatttcacca ggggaaaact catgagcagt 420
 ctgcacctga aaagatatta tgggaggatt ctgcattacc tgaaggccaa ggagtacagt 480
 cactgtgcct ggaccatagt cagagtggaa atcctaagga acttttactt cattaacaga 540
 cttacaggtt acctccgaaa c 561

<210> 481
 <211> 187
 <212> PRT
 <213> Homo sapiens

<400> 481
 Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15
 Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
 20 25 30
 Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
 35 40 45
 Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
 50 55 60
 Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
 65 70 75 80
 Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
 85 90 95
 Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
 100 105 110
 Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
 115 120 125
 Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
 130 135 140
 Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
 145 150 155 160
 His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
 165 170 175

Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
 180 185

<210> 482

<211> 775

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (487)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 482

Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Gly Val Phe Arg Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Xaa His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525

Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
530 535 540

Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
545 550 555 560

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
565 570 575

Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
580 585 590

Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
595 600 605

Leu Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe
610 615 620

Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys
625 630 635 640

Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu
645 650 655

Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu
660 665 670

Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp
675 680 685

Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile
690 695 700

Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe
705 710 715 720

Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly
725 730 735

Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp
740 745 750

Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg
755 760 765

Leu Thr Gly Tyr Leu Arg Asn
770 775

<210> 483

<211> 501

<212> DNA

<213> Homo sapiens

<400> 483

atgagctaca acttgcttgg attcctacaa agaagcagca attttcagtg tcagaagctc 60
ctgtggcaat tgaatgggag gcttgaatat tgcctcaagg acaggatgaa ctttgacatc 120
cctgaggaga ttaagcagct gcagcagttc cagaaggagg acgccgcatt gaccatctat 180

gagatgctcc agaacatctt tgctattttc agacaagatt catctagcac tggctggaat 240
 gagactattg ttgagaacct cctggctaatt gtctatcatc agataaacca tctgaagaca 300
 gtcctggaag aaaaactgga gaaagaagat ttcaccaggg gaaaactcat gagcagtctg 360
 cacctgaaaa gatattatgg gaggattctg cattacctga aggccaaagga gtacagtcac 420
 tgtgcttgga ccatagtcag agtggaaatc ctaaggaact tttacttcat taacagactt 480
 acagggttacc tccgaaacta a 501

<210> 484

<211> 166

<212> PRT

<213> Homo sapiens

<400> 484

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
 100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
 115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160

Thr Gly Tyr Leu Arg Asn
 165

<210> 485

<211> 771

<212> PRT

<213> Homo sapiens

<400> 485

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15

Thr Thr Ala Leu Ser Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser

20										25										30																																		
Ser	Asn	Phe	Gln	Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu																																							
		35					40					45																																										
Glu	Tyr	Cys	Leu	Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile																																							
	50					55					60																																											
Lys	Gln	Leu	Gln	Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr																																							
	65				70					75					80																																							
Glu	Met	Leu	Gln	Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser																																							
				85					90																																													
Thr	Gly	Trp	Asn	Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr																																							
			100					105					110																																									
His	Gln	Ile	Asn	His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys																																							
		115				120						125																																										
Glu	Asp	Phe	Thr	Arg	Gly	Lys	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg																																							
	130					135					140																																											
Tyr	Tyr	Gly	Arg	Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His																																							
	145				150					155					160																																							
Cys	Ala	Trp	Thr	Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Phe																																							
				165				170				175																																										
Ile	Asn	Arg	Leu	Thr	Gly	Tyr	Leu	Arg	Asn	Asp	Ala	His	Lys	Ser	Glu																																							
			180				185					190																																										
Val	Ala	His	Arg	Phe	Lys	Asp	Leu	Gly	Glu	Glu	Asn	Phe	Lys	Ala	Leu																																							
	195					200					205																																											
Val	Leu	Ile	Ala	Phe	Ala	Gln	Tyr	Leu	Gln	Gln	Cys	Pro	Phe	Glu	Asp																																							
	210					215					220																																											
His	Val	Lys	Leu	Val	Asn	Glu	Val	Thr	Glu	Phe	Ala	Lys	Thr	Cys	Val																																							
	225				230				235					240																																								
Ala	Asp	Glu	Ser	Ala	Glu	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe																																							
				245				250				255																																										
Gly	Asp	Lys	Leu	Cys	Thr	Val	Ala	Thr	Leu	Arg	Glu	Thr	Tyr	Gly	Glu																																							
			260				265					270																																										
Met	Ala	Asp	Cys	Cys	Ala	Lys	Gln	Glu	Pro	Glu	Arg	Asn	Glu	Cys	Phe																																							
	275					280					285																																											
Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Asn	Leu	Pro	Arg	Leu	Val	Arg	Pro																																							
	290					295					300																																											
Glu	Val	Asp	Val	Met	Cys	Thr	Ala	Phe	His	Asp	Asn	Glu	Glu	Thr	Phe																																							
	305				310				315					320																																								
Leu	Lys	Lys	Tyr	Leu	Tyr	Glu	Ile	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr																																							

[illegible]

625 630 635 640
 Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
 645 650 655
 Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
 660 665 670
 Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
 675 680 685
 Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
 690 695 700
 Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
 705 710 715 720
 His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp
 725 730 735
 Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
 740 745 750
 Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
 755 760 765
 Leu Gly Leu
 770

<210> 486
 <211> 561
 <212> DNA
 <213> Homo sapiens

<400> 486
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 ctctgtggc aattgaatgg gaggttgaa tattgcctca aggacaggat gaactttgac 180
 atccctgagg agattaagca gctgcagcag ttccagaagg aggacgccgc attgaccatc 240
 tatgagatgc tccagaacat ctttgctatt ttcagacaag attcatctag cactggctgg 300
 aatgagacta ttgttgagaa cctcctggct aatgtctatc atcagataaa ccatctgaag 360
 acagtcctgg aagaaaaact ggagaaagaa gatttcacca ggggaaaact catgagcagt 420
 ctgcacctga aaagatatta tgggaggatt ctgcattacc tgaaggccaa ggagtacagt 480
 cactgtgcct ggaccatagt cagagtggaa atcctaagga acttttactt cattaacaga 540
 cttacagggtt acctccgaaa c 561

<210> 487
 <211> 187
 <212> PRT
 <213> Homo sapiens

<400> 487
 Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15
 Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
 20 25 30

Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
 35 40 45
 Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
 50 55 60
 Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
 65 70 75 80
 Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
 85 90 95
 Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
 100 105 110
 Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
 115 120 125
 Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
 130 135 140
 Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
 145 150 155 160
 His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
 165 170 175
 Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
 180 185

<210> 488

<211> 771

<212> PRT

<213> Homo sapiens

<400> 488

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
 1 5 10 15
 Thr Thr Ala Leu Ser Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser
 20 25 30
 Ser Asn Phe Gln Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu
 35 40 45
 Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile
 50 55 60
 Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr
 65 70 75 80
 Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser
 85 90 95
 Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr
 100 105 110

His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys
 115 120 125
 Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg
 130 135 140
 Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His
 145 150 155 160
 Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe
 165 170 175
 Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn Asp Ala His Lys Ser Glu
 180 185 190
 Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu
 195 200 205
 Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp
 210 215 220
 His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val
 225 230 235 240
 Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe
 245 250 255
 Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu
 260 265 270
 Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
 275 280 285
 Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro
 290 295 300
 Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe
 305 310 315 320
 Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr
 325 330 335
 Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr
 340 345 350
 Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu
 355 360 365
 Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu
 370 375 380
 Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
 385 390 395 400
 Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu
 405 410 415

Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys
 420 425 430
 His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys
 435 440 445
 Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys
 450 455 460
 Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu
 465 470 475 480
 Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val
 485 490 495
 Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
 500 505 510
 Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser
 515 520 525
 Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu
 530 535 540
 Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe
 545 550 555 560
 Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln
 565 570 575
 Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala
 580 585 590
 Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr
 595 600 605
 Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys
 610 615 620
 Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser
 625 630 635 640
 Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
 645 650 655
 Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
 660 665 670
 Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
 675 680 685
 Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
 690 695 700
 Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
 705 710 715 720

His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp
725 730 735

Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
740 745 750

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala
755 760 765

Leu Gly Leu
770

<210> 489

<211> 561

<212> DNA

<213> Homo sapiens

<400> 489

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tccatgagct	acaacttgct	tggattccta	caaagaagca	gcaattttca	gtgtcagaag	120
ctcctgtggc	aattgaatgg	gaggcttgaa	tattgcctca	aggacaggat	gaactttgac	180
atccctgagg	agattaagca	gctgcagcag	ttccagaagg	aggacgccgc	attgaccatc	240
tatgagatgc	tccagaacat	ctttgctatt	ttcagacaag	attcatctag	cactggctgg	300
aatgagacta	ttgttgagaa	cctcctggct	aatgtctatc	atcagataaa	ccatctgaag	360
acagtccctg	aagaaaaact	ggagaaagaa	gatttcacca	gggaaaaact	catgagcagt	420
ctgcacctga	aaagatatta	tgggaggatt	ctgcattacc	tgaaggccaa	ggagtacagt	480
cactgtgcct	ggaccatagt	cagagtggaa	atcctaagga	acttttactt	cattaacaga	540
cttacagggt	acctccgaaa	c				561

<210> 490

<211> 187

<212> PRT

<213> Homo sapiens

<400> 490

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
1 5 10 15

Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
20 25 30

Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
35 40 45

Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
50 55 60

Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
65 70 75 80

Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
85 90 95

Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
100 105 110

Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
 115 120 125
 Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
 130 135 140
 Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
 145 150 155 160
 His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
 165 170 175
 Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
 180 185
 <210> 491
 <211> 769
 <212> PRT
 <213> Homo sapiens
 <400> 491
 Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ala Gly Val
 1 5 10 15
 Ser Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu
 20 25 30
 Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr
 35 40 45
 Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val
 50 55 60
 Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys
 65 70 75 80
 Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala
 85 90 95
 Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln
 100 105 110
 Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
 115 120 125
 Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala
 130 135 140
 Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile
 145 150 155 160
 Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala
 165 170 175
 Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys
 180 185 190

Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys
 195 200 205
 Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe
 210 215 220
 Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg
 225 230 235 240
 Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu
 245 250 255
 Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
 260 265 270
 Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser
 275 280 285
 Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys
 290 295 300
 Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu
 305 310 315 320
 Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn
 325 330 335
 Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr
 340 345 350
 Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala
 355 360 365
 Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro
 370 375 380
 His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu
 385 390 395 400
 Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
 405 410 415
 Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
 420 425 430
 Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
 435 440 445
 Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
 450 455 460
 Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
 465 470 475 480
 Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
 485 490 495

Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
 500 505 510
 Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
 515 520 525
 Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
 530 535 540
 Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
 545 550 555 560
 Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
 565 570 575
 Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
 580 585 590
 Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu Met Ser Tyr Asn Leu
 595 600 605
 Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu
 610 615 620
 Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn
 625 630 635 640
 Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu
 645 650 655
 Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile
 660 665 670
 Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu
 675 680 685
 Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val
 690 695 700
 Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met
 705 710 715 720
 Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu
 725 730 735
 Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu
 740 745 750
 Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg
 755 760 765

Asn

<210> 492

<211> 498

<212> DNA

<213> Homo sapiens

<400> 492
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 ctgtggcaat tgaatgggag gcttgaatat tgcctcaagg acaggatgaa ctttgacatc 120
 cctgaggaga ttaagcagct gcagcagttc cagaaggagg acgccgcatt gaccatctat 180
 gagatgctcc agaacatctt tgctattttc agacaagatt catctagcac tggctggaat 240
 gagactattg ttgagaacct cctggctaatt gtctatcatc agataaacca tctgaagaca 300
 gtcctggaag aaaaactgga gaaagaagat ttcaccaggg gaaaactcat gagcagtcctg 360
 cacctgaaaa gatattatgg gaggattctg cattacctga aggccaagga gtacagtcac 420
 tgtgcctgga ccatagtcag agtggaaatc ctaaggaact tttacttcat taacagactt 480
 acaggttacc tccgaaac 498

<210> 493
 <211> 166
 <212> PRT
 <213> Homo sapiens

<400> 493
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1 5 10 15
 Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20 25 30
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35 40 45
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50 55 60
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65 70 75 80
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85 90 95
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
 100 105 110
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
 115 120 125
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160
 Thr Gly Tyr Leu Arg Asn
 165

<210> 494
 <211> 769
 <212> PRT
 <213> Homo sapiens

<400> 494

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Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Ser Gly Val
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Ser Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu
      20           25           30

Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr
      35           40           45

Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val
      50           55           60

Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys
      65           70           75           80

Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala
      85           90           95

Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln
      100          105          110

Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
      115          120          125

Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala
      130          135          140

Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile
      145          150          155          160

Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala
      165          170          175

Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys
      180          185          190

Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys
      195          200          205

Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe
      210          215          220

Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg
      225          230          235          240

Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu
      245          250          255

Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
      260          265          270

Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser
      275          280          285

Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys
      290          295          300

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Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu
 305 310 315 320
 Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn
 325 330 335
 Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr
 340 345 350
 Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala
 355 360 365
 Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro
 370 375 380
 His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu
 385 390 395 400
 Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
 405 410 415
 Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
 420 425 430
 Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
 435 440 445
 Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
 450 455 460
 Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
 465 470 475 480
 Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
 485 490 495
 Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
 500 505 510
 Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
 515 520 525
 Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
 530 535 540
 Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
 545 550 555 560
 Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
 565 570 575
 Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
 580 585 590
 Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu Met Ser Tyr Asn Leu
 595 600 605

Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu
610 615 620

Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn
625 630 635 640

Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu
645 650 655

Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile
660 665 670

Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu
675 680 685

Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val
690 695 700

Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met
705 710 715 720

Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu
725 730 735

Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu
740 745 750

Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg
755 760 765

Asn

<210> 495

<211> 498

<212> DNA

<213> Homo sapiens

<400> 495

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ctgtggcaat tgaatgggag gcttgaatat tgccctcaagg acaggatgaa ctttgacatc 120
cctgaggaga ttaagcagct gcagcagttc cagaaggagg acgccgcatt gaccatctat 180
gagatgctcc agaacatctt tgctatcttc agacaagatt catctagcac tggctggaat 240
gagactattg ttgagaacct cctggctaata gtctatcatc agataaacca tctgaagaca 300
gtcctggaag aaaaactgga gaaagaagat ttcaccaggg gaaaactcat gagcagtcctg 360
cacctgaaaa gatattatgg gaggattctg cattacctga aggccaagga gtacagtcac 420
tgtgcctgga ccatagtcag agtggaatc ctaaggaaact ttacttcat taacagactt 480
acaggttacc tccgaaac 498

<210> 496

<211> 166

<212> PRT

<213> Homo sapiens

<400> 496

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
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Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20 25 30
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35 40 45
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50 55 60
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65 70 75 80
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85 90 95
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
 100 105 110
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
 115 120 125
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160
 Thr Gly Tyr Leu Arg Asn
 165

<210> 497
 <211> 769
 <212> PRT
 <213> Homo sapiens

<400> 497
 Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Leu Phe Gly Gly Val
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 Ser Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu
 20 25 30
 Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr
 35 40 45
 Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val
 50 55 60
 Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys
 65 70 75 80
 Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala
 85 90 95
 Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln
 100 105 110

Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
 115 120 125
 Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala
 130 135 140
 Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile
 145 150 155 160
 Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala
 165 170 175
 Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys
 180 185 190
 Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys
 195 200 205
 Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe
 210 215 220
 Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg
 225 230 235 240
 Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu
 245 250 255
 Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
 260 265 270
 Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser
 275 280 285
 Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys
 290 295 300
 Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu
 305 310 315 320
 Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn
 325 330 335
 Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr
 340 345 350
 Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala
 355 360 365
 Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro
 370 375 380
 His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu
 385 390 395 400
 Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
 405 410 415

Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
 420 425 430
 Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
 435 440 445
 Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
 450 455 460
 Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
 465 470 475 480
 Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
 485 490 495
 Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
 500 505 510
 Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
 515 520 525
 Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
 530 535 540
 Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
 545 550 555 560
 Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
 565 570 575
 Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
 580 585 590
 Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu Met Ser Tyr Asn Leu
 595 600 605
 Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu
 610 615 620
 Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn
 625 630 635 640
 Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu
 645 650 655
 Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile
 660 665 670
 Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu
 675 680 685
 Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val
 690 695 700
 Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met
 705 710 715 720

Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu
725 730 735

Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu
740 745 750

Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg
755 760 765

Asn

<210> 498

<211> 498

<212> DNA

<213> Homo sapiens

<400> 498

atgagctaca acttgcttgg attcctacaa agaagcagca attttcagtg tcagaagctc 60
ctgtggcaat tgaatgggag gcttgaatat tgcctcaagg acaggatgaa ctttgacatc 120
cctgaggaga ttaagcagct gcagcagttc cagaaggagg acgccgcatt gaccatctat 180
gagatgctcc agaacatctt tgctattttc agacaagatt catctagcac tggctggaat 240
gagactattg ttgagaacct cctgggctaatt gtctatcatc agataaacca tctgaagaca 300
gtcctggaag aaaaactgga gaaagaagat ttcaccaggg gaaaactcat gagcagtcctg 360
cacctgaaaa gatattatgg gaggattctg cattacctga aggccaagga gtacagtcac 420
tgtgcctgga ccatagtcag agtggaatc ctaaggaact tttacttcat taacagactt 480
acaggttacc tccgaaac 498

<210> 499

<211> 166

<212> PRT

<213> Homo sapiens

<400> 499

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
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Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg

115 120 125
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
 130 135 140
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
 145 150 155 160
 Thr Gly Tyr Leu Arg Asn
 165
 <210> 500
 <211> 774
 <212> PRT
 <213> Homo sapiens
 <400> 500
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys

210	215	220
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val 225 230 235 240		
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser 245 250 255		
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly 260 265 270		
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile 275 280 285		
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu 290 295 300		
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp 305 310 315 320		
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser 325 330 335		
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly 340 345 350		
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val 355 360 365		
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys 370 375 380		
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu 385 390 395 400		
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys 405 410 415		
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu 420 425 430		
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val 435 440 445		
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His 450 455 460		
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val 465 470 475 480		
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg 485 490 495		
Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe 500 505 510		
Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala		

515					520					525					
Glu	Thr	Phe	Thr	Phe	His	Ala	Asp	Ile	Cys	Thr	Leu	Ser	Glu	Lys	Glu
530						535					540				
Arg	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Val	Glu	Leu	Val	Lys	His	Lys
545					550					555					560
Pro	Lys	Ala	Thr	Lys	Glu	Gln	Leu	Lys	Ala	Val	Met	Asp	Asp	Phe	Ala
					565					570					575
Ala	Phe	Val	Glu	Lys	Cys	Cys	Lys	Ala	Asp	Asp	Lys	Glu	Thr	Cys	Phe
					580					585					590
Ala	Glu	Glu	Gly	Lys	Lys	Leu	Val	Ala	Ala	Ser	Gln	Ala	Ala	Leu	Gly
					595					600					605
Leu	Cys	Asp	Leu	Pro	Gln	Thr	His	Ser	Leu	Gly	Ser	Arg	Arg	Thr	Leu
					610					615					620
Met	Leu	Leu	Ala	Gln	Met	Arg	Arg	Ile	Ser	Leu	Phe	Ser	Cys	Leu	Lys
					625					630					640
Asp	Arg	His	Asp	Phe	Gly	Phe	Pro	Gln	Glu	Glu	Phe	Gly	Asn	Gln	Phe
					645					650					655
Gln	Lys	Ala	Glu	Thr	Ile	Pro	Val	Leu	His	Glu	Met	Ile	Gln	Gln	Ile
					660					665					670
Phe	Asn	Leu	Phe	Ser	Thr	Lys	Asp	Ser	Ser	Ala	Ala	Trp	Asp	Glu	Thr
					675					680					685
Leu	Leu	Asp	Lys	Phe	Tyr	Thr	Glu	Leu	Tyr	Gln	Gln	Leu	Asn	Asp	Leu
					690					695					700
Glu	Ala	Cys	Val	Met	Gln	Glu	Glu	Arg	Val	Gly	Glu	Thr	Pro	Leu	Met
					705					710					720
Asn	Ala	Asp	Ser	Ile	Leu	Ala	Val	Lys	Lys	Tyr	Phe	Arg	Arg	Ile	Thr
					725					730					735
Leu	Tyr	Leu	Thr	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val
					740					745					750
Arg	Ala	Glu	Ile	Met	Arg	Ser	Leu	Ser	Leu	Ser	Thr	Asn	Leu	Gln	Glu
					755					760					765
Arg	Leu	Arg	Arg	Lys	Glu										
					770										

<210> 501

<211> 495

<212> DNA

<213> Homo sapiens

<400> 501

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 atgaggagaa tctctctttt ctctgcttg aaggacagac atgactttgg atttccccag 120
 gaggagtgtg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgatc 180
 cagcagatct tcaatctctt cagcacaaag gactcatctg ctgcttggga tgagaccctc 240
 ctagacaaat tctacactga actctaccag cagctgaatg acttgggaagc ctgtgtgatg 300
 caggaggaga ggggtgggaga aactcccctg atgaatgcgg actccatctt ggctgtgaag 360
 aaatacttcc gaagaatcac tctctatctg acagagaaga aatacagccc ttgtgcctgg 420
 gaggttgtca gaggagaaat catgagatcc ctctctttat caacaaactt gcaagaaaga 480
 ttaaggagga agga 495

<210> 502

<211> 165

<212> PRT

<213> Homo sapiens

<400> 502

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95

Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met Asn
 100 105 110

Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr Leu
 115 120 125

Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140

Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu Arg
 145 150 155 160

Leu Arg Arg Lys Glu
 165

<210> 503

<211> 38

<212> DNA

<213> Homo sapiens

<400> 503

caagctgcct taggcttatg tgatctgcct caaaccga

38

<210> 504
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 504
 gcgcattggcg cgccttattc cttcctcctt aatctttct

39

<210> 505
 <211> 774
 <212> PRT
 <213> Homo sapiens

<400> 505
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys

210	215	220
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val		
225	230	235 240
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser		
	245	250 255
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly		
	260	265 270
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile		
	275	280 285
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu		
	290	295 300
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp		
305	310	315 320
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser		
	325	330 335
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly		
	340	345 350
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val		
	355	360 365
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys		
	370	375 380
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu		
385	390	395 400
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys		
	405	410 415
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu		
	420	425 430
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val		
	435	440 445
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His		
	450	455 460
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val		
465	470	475 480
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg		
	485	490 495
Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe		
	500	505 510
Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala		

515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu
 610 615 620
 Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys
 625 630 635 640
 Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe
 645 650 655
 Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
 660 665 670
 Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
 675 680 685
 Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
 690 695 700
 Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
 705 710 715 720
 Tyr Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
 725 730 735
 Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val
 740 745 750
 Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Ile Asn Leu Gln Lys
 755 760 765
 Arg Leu Lys Ser Lys Glu
 770

<210> 506

<211> 495

<212> DNA

<213> Homo. sapiens

<400> 506

tgtgatctgc ctcaaaccga cagcctgggt agcaggagga ccttgatgct cctggcacag 60
 atgaggagaa tctctctttt ctctgcttg aaggacagac atgactttgg atttccccag 120
 gaggagtgtg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
 cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttgga tgagaccctc 240
 ctagacaaat tctacactga actctaccag cagctgaatg acctggagtc ctgtgtgatg 300
 caggaagtgg ggggtataga gtctcccctg atgtacgagg actccatcct ggctgtgagg 360
 aaatacttcc aaagaatcac tctatatctg acagagaaga aatacagctc ttgtgcctgg 420
 gaggttgca gagcagaaat catgagatcc ttctctttat caatcaactt gcaaaaaaga 480
 ttgaagagta aggaa 495

<210> 507

<211> 165

<212> PRT

<213> Homo sapiens

<400> 507

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met Tyr
 100 105 110
 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125
 Tyr Leu Thr Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Ile Asn Leu Gln Lys Arg
 145 150 155 160
 Leu Lys Ser Lys Glu
 165

<210> 508

<211> 38

<212> DNA

<213> Homo sapiens

<400> 508
caagctgcct taggcttatg tgatctgcct caaaccca 38

<210> 509
<211> 38
<212> DNA
<213> Homo sapiens

<400> 509
gcgcattggcg cgcctcattc cttactcttc aatctttt 38

<210> 510
<211> 774
<212> PRT
<213> Homo sapiens

<400> 510
Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15
Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
20 25 30
His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
35 40 45
Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
50 55 60
Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
65 70 75 80
Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
85 90 95
Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
100 105 110
Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
115 120 125
His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
130 135 140
Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
145 150 155 160
Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
165 170 175
Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
180 185 190
Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
195 200 205
Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys

210	215	220
Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val 225 230 235 240		
Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser 245 250 255		
Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly 260 265 270		
Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile 275 280 285		
Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu 290 295 300		
Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp 305 310 315 320		
Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser 325 330 335		
Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly 340 345 350		
Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val 355 360 365		
Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys 370 375 380		
Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu 385 390 395 400		
Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys 405 410 415		
Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu 420 425 430		
Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val 435 440 445		
Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His 450 455 460		
Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val 465 470 475 480		
Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg 485 490 495		
Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe 500 505 510		
Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala		

515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu
 610 615 620
 Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys
 625 630 635 640
 Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe
 645 650 655
 Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
 660 665 670
 Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
 675 680 685
 Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Met
 690 695 700
 Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
 705 710 715 720
 Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
 725 730 735
 Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
 740 745 750
 Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Lys Ile Phe Gln Glu
 755 760 765
 Arg Leu Arg Arg Lys Glu
 770
 <210> 511
 <211> 495
 <212> DNA
 <213> Homo sapiens
 <400> 511
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atgaggagaa tctctctttt ctctgcttg aaggacagac atgacttttg atttccccag 120
gaggagtttg gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgatc 180
cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttgga tgagaccctc 240
ctagacaaat tctacactga actctaccag cagctgaatg acatggaagc ctgctgtgata 300
caggaggttg ggggtggaaga gactcccctg atgaatgtgg actccatctt ggctgtgaag 360
aaatacttcc aaagaatcac tctttatctg acagagaaga aatacagccc ttgtgcttgg 420
gaggttgtca gaggagaaat catgagatcc ttctctttat caaaaatttt tcaagaaaga 480
ttaaggagga aggaa 495

<210> 512

<211> 165

<212> PRT

<213> Homo sapiens

<400> 512

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Met Glu
85 90 95

Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met Asn
100 105 110

Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125

Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Lys Ile Phe Gln Glu Arg
145 150 155 160

Leu Arg Arg Lys Glu
165

<210> 513

<211> 38

<212> DNA

<213> Homo sapiens

<400> 513

caagctgcct taggcttatg tgatctgcct caaaccca

38

<210> 514
 <211> 39
 <212> DNA
 <213> Homo sapiens

<400> 514
 gcgcgatggcg cgccttatcc ctctctcctt aatctttct

39

<210> 515
 <211> 774
 <212> PRT
 <213> Homo sapiens

<400> 515

Met	Lys	Trp	Val	Ser	Phe	Ile	Ser	Leu	Leu	Phe	Leu	Phe	Ser	Ser	Ala	
1				5					10					15		
Tyr	Ser	Arg	Ser	Leu	Asp	Lys	Arg	Asp	Ala	His	Lys	Ser	Glu	Val	Ala	
			20					25					30			
His	Arg	Phe	Lys	Asp	Leu	Gly	Glu	Glu	Asn	Phe	Lys	Ala	Leu	Val	Leu	
		35					40					45				
Ile	Ala	Phe	Ala	Gln	Tyr	Leu	Gln	Gln	Cys	Pro	Phe	Glu	Asp	His	Val	
	50					55					60					
Lys	Leu	Val	Asn	Glu	Val	Thr	Glu	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	
65					70					75				80		
Glu	Ser	Ala	Glu	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	
			85						90					95		
Lys	Leu	Cys	Thr	Val	Ala	Thr	Leu	Arg	Glu	Thr	Tyr	Gly	Glu	Met	Ala	
			100					105					110			
Asp	Cys	Cys	Ala	Lys	Gln	Glu	Pro	Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	
		115					120				125					
His	Lys	Asp	Asp	Asn	Pro	Asn	Leu	Pro	Arg	Leu	Val	Arg	Pro	Glu	Val	
	130					135					140					
Asp	Val	Met	Cys	Thr	Ala	Phe	His	Asp	Asn	Glu	Glu	Thr	Phe	Leu	Lys	
145				150					155					160		
Lys	Tyr	Leu	Tyr	Glu	Ile	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	
			165						170					175		
Glu	Leu	Leu	Phe	Phe	Ala	Lys	Arg	Tyr	Lys	Ala	Ala	Phe	Thr	Glu	Cys	
		180					185						190			
Cys	Gln	Ala	Ala	Asp	Lys	Ala	Ala	Cys	Leu	Leu	Pro	Lys	Leu	Asp	Glu	
	195					200						205				
Leu	Arg	Asp	Glu	Gly	Lys	Ala	Ser	Ser	Ala	Lys	Gln	Arg	Leu	Lys	Cys	
	210					215					220					

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525

Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu
 610 615 620
 Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys
 625 630 635 640
 Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe
 645 650 655
 Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
 660 665 670
 Phe Asn Leu Phe Thr Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp
 675 680 685
 Leu Leu Asp Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
 690 695 700
 Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
 705 710 715 720
 Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
 725 730 735
 Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
 740 745 750
 Arg Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu
 755 760 765
 Arg Leu Arg Arg Lys Glu
 770

<210> 516

<211> 495

<212> DNA

<213> Homo sapiens

<400> 516

tgtgatctgc ctcaaaccga cagcctgggt agcaggagga ccttgatgct cctggcacag 60

atgaggagaa tctctctttt ctctgcttg aaggacagac atgactttgg atttcccag 120
 gaggagttt gcaaccagtt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgac 180
 cagcagatct tcaacctctt taccacaaaa gattcatctg ctgcttgga tgaggacctc 240
 ctagacaaat tctgcaccga actctaccag cagctgaatg acttggaagc ctgtgtgatg 300
 caggaggaga ggggtgggaga aactcccctg atgaatgcgg actccatctt ggctgtgaag 360
 aaatacttcc gaagaatcac tctctatctg acagagaaga aatacagccc ttgtgcctgg 420
 gaggttgca gagcagaaat catgagatcc ctctctttat caacaaactt gcaagaaaga 480
 ttaaggagga aggaa 495

<210> 517

<211> 165

<212> PRT

<213> Homo sapiens

<400> 517

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60

Asn Leu Phe Thr Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp Leu
 65 70 75 80

Leu Asp Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95

Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met Asn
 100 105 110

Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr Leu
 115 120 125

Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140

Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu Arg
 145 150 155 160

Leu Arg Arg Lys Glu
 165

<210> 518

<211> 38

<212> DNA

<213> Homo sapiens

<400> 518

caagctgcct taggcttatg tgatctgcct caaaccca

38

<210> 519

<211> 39
 <212> DNA
 <213> Homo sapiens

<400> 519
 gcgcattggcg cgccttattc cttcctcctt aatctttct

39

<210> 520
 <211> 774
 <212> PRT
 <213> Homo sapiens

<400> 520
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540

Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu
 610 615 620
 Met Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys
 625 630 635 640
 Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe
 645 650 655
 Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
 660 665 670
 Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
 675 680 685
 Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
 690 695 700
 Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
 705 710 715 720
 Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
 725 730 735
 Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
 740 745 750
 Arg Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu
 755 760 765
 Arg Leu Arg Arg Lys Glu
 770

<210> 521

<211> 495

<212> DNA

<213> Homo sapiens

<400> 521

tgtgatctgc ctcaaaccga cagcctgggt agcaggagga ccttgatgct cctggcacag 60
 atgaggagaa tctctctttt ctctgcttg aaggacagac atgacttttg atttccccag 120
 gaggagtttg gcaaccagt ccaaaaggct gaaaccatcc ctgtcctcca tgagatgatc 180
 cagcagatct tcaatctctt cagcacaag gactcatctg ctgcttgga tgagaccctc 240

ctagacaaat tctacactga actctaccag cagctgaatg acttggaagc ctgtgtgatg 300
 caggaggaga ggggtgggaga aactccccctg atgaatgcgg actccatctt ggctgtgaag 360
 aaatacttcc gaagaatcac tctctatctg acagagaaga aatacagccc ttgtgcctgg 420
 gaggttgtca gagcagaaat catgagatcc ctctctttat caacaaactt gcaagaaaga 480
 ttaaggagga aggaa 495

<210> 522

<211> 165

<212> PRT

<213> Homo sapiens

<400> 522

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95

Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met Asn
 100 105 110

Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr Leu
 115 120 125

Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140

Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu Arg
 145 150 155 160

Leu Arg Arg Lys Glu
 165

<210> 523

<211> 21

<212> DNA

<213> Homo sapiens

<400> 523

agaagtgtg caaggctgac g

21

<210> 524

<211> 20

<212> DNA

<213> Homo sapiens

<400> 524

acctgaccta caggaaagag

20

<210> 525

<211> 742

<212> PRT

<213> Homo sapiens

<400> 525

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15Tyr Ser Arg Ser Leu Asp Lys Arg Ala Pro Thr Ser Ser Ser Thr Lys
20 25 30Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile
35 40 45Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu
50 55 60Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu
65 70 75 80Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu
85 90 95Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn
100 105 110Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met
115 120 125Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg
130 135 140Trp Ile Thr Phe Ser Gln Ser Ile Ile Ser Thr Leu Thr Asp Ala His
145 150 155 160Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
165 170 175Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
180 185 190Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
195 200 205Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
210 215 220Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
225 230 235 240

Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn

245	250	255
Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu		
260	265	270
Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu		
275	280	285
Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro		
290	295	300
Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala		
305	310	315
Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu		
325	330	335
Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys		
340	345	350
Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe		
355	360	365
Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu		
370	375	380
Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr		
385	390	395
Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp		
405	410	415
Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu		
420	425	430
Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala		
435	440	445
Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala		
450	455	460
Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys		
465	470	475
Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro		
485	490	495
Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr		
500	505	510
Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala		
515	520	525
Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu		
530	535	540
Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe		

545 550 555 560
 Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
 565 570 575
 Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
 580 585 590
 Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
 595 600 605
 Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
 610 615 620
 Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
 625 630 635 640
 Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
 645 650 655
 Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
 660 665 670
 Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
 675 680 685
 Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
 690 695 700
 Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
 705 710 715 720
 Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
 725 730 735
 Gln Ala Ala Leu Gly Leu
 740

<210> 526

<211> 462

<212> DNA

<213> Homo sapiens

<400> 526

atgtacagga	tgcaactcct	gtcttgcat	gcactaagtc	ttgcacttgt	cacaaacagt	60
gcacctactt	caagttctac	aaagaaaaca	cagctacaac	tggagcattt	actgctggat	120
ttacagatga	ttttgaatgg	aattaataat	tacaagaatc	ccaaactcac	caggatgctc	180
acatttaagt	tttacctgcc	caagaaggcc	acagaactga	aacatcttca	gtgtctagaa	240
gaagaactca	aacctctgga	ggaagtgcta	aatttagctc	aaagcaaaaa	ctttcactta	300
agaccaggga	acttaatcag	caatatcaac	gtaatagttc	tggaactaaa	gggatctgaa	360
acaacattca	tgtgtgaata	tgctgatgag	acagcaacca	ttgtagaatt	tctgaacaga	420
tggattacct	tttgtcaaag	catcatctca	acactgactt	ga		462

<210> 527

<211> 153

<212> PRT

<213> Homo sapiens

<400> 527

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15
 Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Cys Gln Ser Ile Ile Ser Thr Leu Thr
 145 150

<210> 528

<211> 742

<212> PRT

<213> Homo sapiens

<400> 528

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400



Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser V: Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu
 610 615 620
 His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr
 625 630 635 640
 Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro
 645 650 655
 Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu
 660 665 670
 Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His
 675 680 685
 Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu
 690 695 700

Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr
705 710 715 720

Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Ser Gln Ser
725 730 735

Ile Ile Ser Thr Leu Thr
740

<210> 529

<211> 462

<212> DNA

<213> Homo sapiens

<400> 529

atgtacagga	tgcaactcct	gtcttgcatt	gcactaagtc	ttgcacttgt	cacaaacagt	60
gcacctactt	caagttctac	aaagaaaaca	cagctacaac	tgagcattt	actgctggat	120
ttacagatga	ttttgaatgg	aattaataat	tacaagaatc	ccaaactcac	caggatgctc	180
acattttaagt	tttcatgcc	caagaaggcc	acagaactga	aacatcttca	gtgtctagaa	240
gaagaactca	aacctctgga	ggaagtgcta	aatttagctc	aaagcaaaaa	ctttcactta	300
agaccaggg	acttaatcag	caatatcaac	gtaatagttc	tggaactaaa	gggatctgaa	360
acaacattca	tgtgtgaata	tgctgatgag	acagcaacca	ttgtagaatt	tctgaacaga	420
tggtattac	cttgcctc	catcatctca	acactgactt	ga		462

<210> 530

<211> 153

<212> PRT

<213> Homo sapiens

<400> 530

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr
145 150

<210> 531

<211> 742

<212> PRT

<213> Homo sapiens

<400> 531

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Ala Pro Thr Ser Ser Ser Thr Lys
20 25 30

Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile
35 40 45

Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu
50 55 60

Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu
65 70 75 80

Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu
85 90 95

Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn
100 105 110

Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met
115 120 125

Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg
130 135 140

Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Asp Ala His
145 150 155 160

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
165 170 175

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
180 185 190

Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
195 200 205

Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
210 215 220

Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
225 230 235 240

Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
245 250 255

Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 260 265 270
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 275 280 285
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
 290 295 300
 Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
 305 310 315 320
 Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
 325 330 335
 Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
 340 345 350
 Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
 355 360 365
 Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
 370 375 380
 Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
 385 390 395 400
 Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
 405 410 415
 Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
 420 425 430
 Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
 435 440 445
 Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
 450 455 460
 Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
 465 470 475 480
 Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
 485 490 495
 Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
 500 505 510
 Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
 515 520 525
 Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
 530 535 540
 Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
 545 550 555 560

Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
565 570 575

Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
580 585 590

Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
595 600 605

Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
610 615 620

Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
625 630 635 640

Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
645 650 655

Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
660 665 670

Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
675 680 685

Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
690 695 700

Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
705 710 715 720

Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
725 730 735

Gln Ala Ala Leu Gly Leu
740

<210> 532

<211> 462

<212> DNA

<213> Homo sapiens

<400> 532

atgtacagga	tgcaactcct	gtcttgcat	gcactaagtc	ttgcacttgt	cacaaacagt	60
gcacctactt	caagttctac	aaagaaaaca	cagctacaac	tgagcattt	actgctggat	120
ttacagatga	ttttgaatgg	aattaataat	tacaagaatc	ccaaactcac	caggatgctc	180
acatttaagt	tttacctgcc	caagaaggcc	acagaactga	aacatcttca	gtgtctagaa	240
gaagaactca	aacctctgga	ggaagtgcta	aatttagctc	aaagcaaaaa	ctttcactta	300
agacccaggg	acttaatcag	caatatcaac	gtaatagttc	tggaactaaa	gggatctgaa	360
acaacattca	tgtgtgaata	tgctgatgag	acagcaacca	ttgtagaatt	tctgaacaga	420
tggtattac	cttgcataag	catcatctca	acactgactt	ga		462

<210> 533

<211> 153

<212> PRT

<213> Homo sapiens

<400> 533

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr
 145 150

<210> 534

<211> 742

<212> PRT

<213> Homo sapiens

<400> 534

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415

Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu
 610 615 620
 His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr
 625 630 635 640
 Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro
 645 650 655
 Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu
 660 665 670
 Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His
 675 680 685
 Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu
 690 695 700
 Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr
 705 710 715 720

Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser
725 730 735

Ile Ile Ser Thr Leu Thr
740

<210> 535

<211> 462

<212> DNA

<213> Homo sapiens

<400> 535

atgtacagga	tgcaactcct	gtcttgcat	gcactaagtc	ttgcacttgt	cacaaacagt	60
gcacctactt	caagttctac	aaagaaaaca	cagctacaac	tggagcattt	actgctggat	120
ttacagatga	ttttgaatgg	aattaataat	tacaagaatc	ccaaactcac	caggatgctc	180
acatttaagt	tttcatgccc	caagaaggcc	acagaactga	aacatcttca	gtgtctagaa	240
gaagaactca	aacctctgga	ggaagtgcta	aatttagctc	aaagcaaaaa	ctttcactta	300
agacccaggg	acttaatcag	caatatcaac	gtaatagttc	tggaactaaa	gggatctgaa	360
acaacattca	tgtgtgaata	tgctgatgag	acagcaacca	ttgtagaatt	tctgaacaga	420
tggtattcct	tttgtcaaag	catcatctca	acactgactt	ga		462

<210> 536

<211> 153

<212> PRT

<213> Homo sapiens

<400> 536

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu	
1 5 10 15	
Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu	
20 25 30	
Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile	
35 40 45	
Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe	
50 55 60	
Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu	
65 70 75 80	
Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys	
85 90 95	
Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile	
100 105 110	
Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala	
115 120 125	
Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe	
130 135 140	
Cys Gln Ser Ile Ile Ser Thr Leu Thr	
145 150	

<210> 537

<211> 738

<212> PRT

<213> Homo sapiens

<400> 537

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Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1             5             10             15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
          20             25             30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
          35             40             45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
          50             55             60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
          65             70             75             80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
          85             90             95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
          100            105            110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
          115            120            125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
          130            135            140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Asp Ala His Lys Ser Glu Val
          145            150            155            160

Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
          165            170            175

Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
          180            185            190

Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
          195            200            205

Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
          210            215            220

Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
          225            230            235            240

Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
          245            250            255

Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
          260            265            270

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Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
 275 280 285
 Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
 290 295 300
 Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
 305 310 315 320
 Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
 325 330 335
 Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
 340 345 350
 Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 355 360 365
 Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
 370 375 380
 Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
 385 390 395 400
 Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
 405 410 415
 Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
 420 425 430
 Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
 435 440 445
 Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu
 450 455 460
 Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
 465 470 475 480
 Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val
 485 490 495
 Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys
 500 505 510
 Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp
 515 520 525
 Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn
 530 535 540
 Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu
 545 550 555 560
 Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu
 565 570 575

Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys
 580 585 590
 His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val
 595 600 605
 Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp
 610 615 620
 Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys
 625 630 635 640
 Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn
 645 650 655
 Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
 660 665 670
 Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His
 675 680 685
 Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
 690 695 700
 Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys
 705 710 715 720
 Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu
 725 730 735

Gly Leu

<210> 538
 <211> 453
 <212> DNA
 <213> Homo sapiens

<400> 538
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 tcaagttcta caaagaaaac acagctacaa ctggagcatt tactgctgga ttacagatg 120
 attttgaatg gaattaataa ttacaagaat cccaaactca ccaggatgct cacatttaag 180
 ttttcatatgc ccaagaaggc cacagaactg aaacatcttc agtgtctaga agaagaactc 240
 aaacctctgg aggaagtgtc aaatttagct caaagcaaaa actttcactt aagaccagg 300
 gacttaatca gcaatatcaa cgtaatatgt ctggaactaa agggatctga aacaacattc 360
 atgtgtgaat atgctgatga gacagcaacc attgtagaat ttctgaacag atggattacc 420
 ttttctcaga gcatcatctc aacactgact tga 453

<210> 539
 <211> 153
 <212> PRT
 <213> Homo sapiens

<400> 539
 Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Ser Gln Ser Ile Ile Ser Thr Leu Thr
 145 150

<210> 540

<211> 738

<212> PRT

<213> Homo sapiens

<400> 540

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15
 Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Cys Gln Ser Ile Ile Ser Thr Leu Thr Asp Ala His Lys Ser Glu Val
 145 150 155 160
 Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
 165 170 175
 Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
 180 185 190
 Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
 195 200 205
 Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
 210 215 220
 Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
 225 230 235 240
 Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
 245 250 255
 Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
 260 265 270
 Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
 275 280 285
 Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
 290 295 300
 Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
 305 310 315 320
 Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
 325 330 335
 Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
 340 345 350
 Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
 355 360 365
 Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
 370 375 380
 Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
 385 390 395 400
 Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
 405 410 415
 Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
 420 425 430

Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
 435 440 445
 Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu
 450 455 460
 Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
 465 470 475 480
 Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val
 485 490 495
 Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys
 500 505 510
 Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp
 515 520 525
 Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn
 530 535 540
 Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu
 545 550 555 560
 Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu
 565 570 575
 Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys
 580 585 590
 His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val
 595 600 605
 Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp
 610 615 620
 Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys
 625 630 635 640
 Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn
 645 650 655
 Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
 660 665 670
 Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His
 675 680 685
 Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
 690 695 700
 Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys
 705 710 715 720
 Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu
 725 730 735

Gly Leu

<210> 541
 <211> 453
 <212> DNA
 <213> Homo sapiens

<400> 541
 atgcaactcc tgtcttgcac tgcactaagt cttgcacttg tcacaaacag tgcacctact 60
 tcaagttcta caaagaaaac acagctacaa ctggagcatt tactgctgga ttacagatg 120
 attttgaatg gaattaataa ttacaagaat cccaaactca ccaggatgct cacatttaag 180
 ttttcatgac ccaagaaggc cacagaactg aaacatcttc agtgtctaga agaagaactc 240
 aaacctctgg aggaagtgc aaatttagct caaagcaaaa actttcactt aagaccagg 300
 gacttaatca gcaatatcaa cgtaatatgt ctggaactaa agggatctga aacaacattc 360
 atgtgtgaat atgctgatga gacagcaacc attgtagaat ttctgaacag atggattacc 420
 ttttctcaga gcatcatctc aacactgact tga 453

<210> 542
 <211> 153
 <212> PRT
 <213> Homo sapiens

<400> 542
 Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15
 Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Ser Gln Ser Ile Ile Ser Thr Leu Thr
 145 150

<210> 543
 <211> 742
 <212> PRT
 <213> Homo sapiens

<400> 543

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ala Pro Thr Ser Ser Ser Thr Lys
 20 25 30
 Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile
 35 40 45
 Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu
 50 55 60
 Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu
 65 70 75 80
 Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu
 85 90 95
 Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn
 100 105 110
 Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met
 115 120 125
 Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg
 130 135 140
 Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr Asp Ala His
 145 150 155 160
 Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
 165 170 175
 Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
 180 185 190
 Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
 195 200 205
 Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
 210 215 220
 Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
 225 230 235 240
 Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
 245 250 255
 Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
 260 265 270
 Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
 275 280 285
 Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro

290	295	300
Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala 305 310 315 320		
Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu 325 330 335		
Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys 340 345 350		
Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe 355 360 365		
Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu 370 375 380		
Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr 385 390 395 400		
Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp 405 410 415		
Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu 420 425 430		
Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala 435 440 445		
Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala 450 455 460		
Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys 465 470 475 480		
Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro 485 490 495		
Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr 500 505 510		
Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala 515 520 525		
Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu 530 535 540		
Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe 545 550 555 560		
Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser 565 570 575		
Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser 580 585 590		
Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp		

595 600 605

Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
610 615 620

Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
625 630 635 640

Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
645 650 655

Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
660 665 670

Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
675 680 685

Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
690 695 700

Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
705 710 715 720

Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
725 730 735

Gln Ala Ala Leu Gly Leu
740

<210> 544

<211> 462

<212> DNA

<213> Homo sapiens

<400> 544

atgtacagaa	tgcaattggt	gtcttgatt	gctttgtctt	tggctttggt	tactaactct	60
gctccaactt	cttcttctac	taagaagact	caattgcaat	tggaacactt	gttggtggac	120
ttgcaaatga	tcttaaacgg	tataaacaac	tataaaaacc	caaagttgac	tagaatgttg	180
actttcaagt	tctacatgcc	aaagaaagct	actgaattga	agcacttgca	atgtttgga	240
gaagaattga	agccattgga	agaagttttg	aacttggctc	aatctaagaa	cttcacttg	300
agaccaagag	atttgatttc	taacattaac	gttattgttt	tggaattgaa	gggttctgaa	360
actactttta	tgtgcgagta	cgcagacgaa	actgctacta	tcgttgagtt	cttaaataagg	420
tggtactactt	tctgccaatc	tattatttct	actttgacat	aa		462

<210> 545

<211> 153

<212> PRT

<213> Homo sapiens

<400> 545

Met	Tyr	Arg	Met	Gln	Leu	Leu	Ser	Cys	Ile	Ala	Leu	Ser	Leu	Ala	Leu
1				5					10				15		
Val	Thr	Asn	Ser	Ala	Pro	Thr	Ser	Ser	Ser	Thr	Lys	Lys	Thr	Gln	Leu
		20					25						30		
Gln	Leu	Glu	His	Leu	Leu	Leu	Asp	Leu	Gln	Met	Ile	Leu	Asn	Gly	Ile

35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Cys Gln Ser Ile Ile Ser Thr Leu Thr
 145 150
 <210> 546
 <211> 742
 <212> PRT
 <213> Homo sapiens
 <400> 546
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140
 Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys

145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445
 Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His

450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu
 610 615 620
 His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr
 625 630 635 640
 Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro
 645 650 655
 Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu
 660 665 670
 Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His
 675 680 685
 Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu
 690 695 700
 Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr
 705 710 715 720
 Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser
 725 730 735
 Ile Ile Ser Thr Leu Thr
 740

<210> 547

<211> 462
 <212> DNA
 <213> Homo sapiens

<400> 547
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 gctccaactt cttcttctac taagaagact caattgcaat tggaacactt gttgttggac 120
 ttgcaaata tcttaaacgg tataaacaac tataaaaacc caaagttgac tagaatgttg 180
 actttcaagt tctacatgcc aaagaaagct actgaattga agcacttgca atgtttggaa 240
 gaagaattga agccattgga agaagttttg aacttggctc aatctaagaa cttccacttg 300
 agaccaagag atttgatttc taacattaac gttattgttt tggaattgaa gggttctgaa 360
 actactttta tgtgcgagta cgcagacgaa actgctacta tcgttgagtt cttaaatagg 420
 tggatcactt tctgccaatc tattatttct actttgacat aa 462

<210> 548
 <211> 153
 <212> PRT
 <213> Homo sapiens

<400> 548
 Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15
 Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Cys Gln Ser Ile Ile Ser Thr Leu Thr
 145 150

<210> 549
 <211> 27
 <212> PRT
 <213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (1)

<223> Xaa equals thiopropionic acid (Tpa)

<220>

<221> MISC_FEATURE

<222> (23)

<223> Xaa equals biphenylalanine (Bip)

<400> 549

Xaa Asn Leu His Phe Cys Gln Leu Arg Cys Lys Ser Leu Gly Leu Leu

1

5

10

15

Gly Lys Cys Ala Gly Ser Xaa Cys Ala Cys Val

20

25

<210> 550

<211> 21

<212> PRT

<213> Homo sapiens

<400> 550

Met Trp Trp Arg Leu Trp Trp Leu Leu Leu Leu Leu Leu Trp

1

5

10

15

Pro Met Val Trp Ala

20

<210> 551

<211> 84

<212> DNA

<213> Homo sapiens

<400> 551

agtgggtgcc ttcctccgc tccagcggca ccacgtccgg cactgcgtgc tcaacgagct

60

ggcccagctg ggcctggagc caag

84

<210> 552

<211> 84

<212> DNA

<213> Homo sapiens

<400> 552

agtgggtgcc ttcctccgc tccagcggca ccacgtccgg cactgcgtgc tcaacgagct

60

ggcccagctg ggcctggagc caag

84

<210> 553

<211> 87

<212> DNA

<213> Homo sapiens

<400> 553

agtgggtgcc ttcctccgc tccagcggca ccacgtccgg cactgcgtgc tcaacgagct

60

ggcccagctg ggcctggagc caagga

87

<210> 554

<211> 87
 <212> DNA
 <213> Homo sapiens

<400> 554
 agtgggtgcc ttcctcccgc tccagcggca ccacgtccgg cactgcgtgc tcaacgagct 60
 ggcccagctg ggcctggagc caaggga 87

<210> 555
 <211> 60
 <212> DNA
 <213> Homo sapiens

<400> 555
 gccatcttca tcttcatcag atggcttctc aaactcgggc atcatggaag agcgcctcct 60

<210> 556
 <211> 60
 <212> DNA
 <213> Homo sapiens

<400> 556
 gccatcttca tcttcatcag atggcttctc aaactcgggc atcatggaag agcgcctcct 60

<210> 557
 <211> 637
 <212> PRT
 <213> Homo sapiens

<400> 557
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
 20 25 30
 His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
 35 40 45
 Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
 50 55 60
 Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
 65 70 75 80
 Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
 85 90 95
 Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
 100 105 110
 Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
 115 120 125
 His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
 130 135 140

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
 145 150 155 160
 Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
 165 170 175
 Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
 180 185 190
 Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
 195 200 205
 Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
 210 215 220
 Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
 225 230 235 240
 Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
 245 250 255
 Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
 260 265 270
 Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
 275 280 285
 Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
 290 295 300
 Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
 305 310 315 320
 Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
 325 330 335
 Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
 340 345 350
 Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
 355 360 365
 Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
 370 375 380
 Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
 385 390 395 400
 Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
 405 410 415
 Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
 420 425 430
 Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
 435 440 445

Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
 450 455 460
 Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
 465 470 475 480
 Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
 485 490 495
 Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
 500 505 510
 Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
 515 520 525
 Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu
 530 535 540
 Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
 545 550 555 560
 Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala
 565 570 575
 Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe
 580 585 590
 Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly
 595 600 605
 Leu Ser Gly Ala Leu Pro Pro Ala Pro Ala Ala Pro Arg Pro Ala Leu
 610 615 620
 Arg Ala Gln Arg Ala Gly Pro Ala Gly Pro Gly Ala Lys
 625 630 635

<210> 558

<211> 637

<212> PRT

<213> Homo sapiens

<400> 558

Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg Ser Gly Ala Leu Pro Pro Ala Pro
 20 25 30
 Ala Ala Pro Arg Pro Ala Leu Arg Ala Gln Arg Ala Gly Pro Ala Gly
 35 40 45
 Pro Gly Ala Lys Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys
 50 55 60
 Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala

65		70		75		80
Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn						
		85		90		95
Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu						
		100		105		110
Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr						
		115		120		125
Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala						
		130		135		140
Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp						
		145		150		155
Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys						
		165		170		175
Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr						
		180		185		190
Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe						
		195		200		205
Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala						
		210		215		220
Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu						
		225		230		235
Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln						
		245		250		255
Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser						
		260		265		270
Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr						
		275		280		285
Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu						
		290		295		300
Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln						
		305		310		315
Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu						
		325		330		335
Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala						
		340		345		350
Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys						
		355		360		365
Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr						

370 375 380
 Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg
 385 390 395 400
 Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala
 405 410 415
 Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu
 420 425 430
 Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu
 435 440 445
 Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr
 450 455 460
 Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg
 465 470 475 480
 Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys
 485 490 495
 Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu
 500 505 510
 Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys
 515 520 525
 Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu
 530 535 540
 Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr
 545 550 555 560
 Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys
 565 570 575
 Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr
 580 585 590
 Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu
 595 600 605
 Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
 610 615 620
 Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
 625 630 635

<210> 559

<211> 638

<212> PRT

<213> Homo sapiens

<400> 559

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Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1              5              10              15

Tyr Ser Arg Ser Leu Asp Lys Arg Asp Ala His Lys Ser Glu Val Ala
      20              25              30

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
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(19) World Intellectual Property
Organization
International Bureau



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C07H 21/04, C07K 14/765, C12P 21/02, 21/04

(21) International Application Number:
PCT/US2004/001369

(22) International Filing Date: 20 January 2004 (20.01.2004)

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60/476,267 6 June 2003 (06.06.2003) US
60/505,172 24 September 2003 (24.09.2003) US
60/506,746 30 September 2003 (30.09.2003) US

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(72) Inventors; and

(75) Inventors/Applicants (for US only): **HASELTINE,
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DC 20007 (US). **ROSEN, Craig, A.** [US/US]; 22400
Rolling Hill Lane, Laytonville, MD 20882 (US).

(74) Agents: **HOOVER?, Kenley, K.?** et al.; 14200 Shady
Grove Road, Rockville, MD 20850 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
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Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
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GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the International search report:
21 April 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **ALBUMIN FUSION PROTEINS**

(57) Abstract: The present invention encompasses albumin fusion proteins. Nucleic acid molecules encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Additionally the present invention encompasses pharmaceutical compositions comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

WO 2005/003296 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/01369

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61 K 38/38; C07 H 21/04; C07 K 14/765; C12 P 21/02,21/04
US CL : 536/23.5; 435/320.1, 325,69.7; 530/363

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5; 435/320.1, 325,69.7; 530/363

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,766,883 B (BALLANCE LL et al) 16 June 1998 (16.06.1999), especially SEQ.ID.NO:14	1-12 and 26
X	WO 02-97038 A2(BELL et al) 05 December, 2002 (05.12.2002), especially SEQ.ID.NO:7	1-12 and 26

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

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A document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
E earlier application or patent published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
O document referring to an oral disclosure, use, exhibition or other means	*Z* document member of the same patent family
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

25 September 2004 (25.09.2004)

Date of mailing of the international search report

24 FEB 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 872-9306

Authorized officer

Patricia Bell Harrison

Telephone No. 571-272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/01369

Continuation of B. FIELDS SEARCHED Item 3:

MEDLINE, STN, A -GENSEQ, N-GENSEQ, EST, DERWENT, SWISS-PROT, PIR, USPTOWEST, SWISSPTREMBL,
GENEMBL, PUBLISHED APPLICATIONS AND ISSUED PATENTS

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